BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 33.] 1936. [No. 10.

PELLAGRA AND PELLAGRA-LIKE CONDITIONS IN WARM CLIMATES.

By Hugh S. STANNUS, PhD., M.D., F.R.C.P.,

Sectional Editor, Tropical Diseases Bulletin.

SECTION I.*

It is just over two hundred years ago that the malady which later became known as Pellagra was first the object of study. During two centuries endemic pellagra has waxed and waned and then again flared up; of very considerable economic importance, the object of many observations, the subject of numerous investigations, the theme of divers theorizations, the disease remains to-day very much what it was in 1931 when R. H. TURNER remarked that "Pellagra (was) unique in the scarcity of accurate information, etiology uncertain, pathology obscure, diagnosis a matter of opinion, criteria of cure unknown, cause of death not understood."

The attention of Gaspar CASAL, a physician of Oviedo, was first drawn to the sickness about 1730, then known to the peasantry of the province of Asturia in North-West Spain as *Mal de la Rosa*.

About 1755 the disease was recognized under the name *Scorbuto Alpino* by Antonio PUJATI of Venice among the inhabitants of the village of Feltre in the province of Belluno but no account of the disease was published in Italy until Francesco FRAPOLLI of Milan set forth, in 1771, his observations made in Lombardy—"Animadversiones in morbum VULGO PELAGRAM"—thus introducing the name by which this scourge was known to the local peasants.

What had happened in Spain and Italy then happened in France. In 1829 Gustave HAMEAU, a country practitioner living in the Teste-de-Buch district, communicated to the Royal Society of Medicine, Bordeaux, observations he had been collecting during the previous ten years upon an affection among the miserable inhabitants living just to the south of the Bay of Arcachon which later proved to be none other than pellagra.

In the latter half of the century it was recognized successively in most of the southern states of Europe, then Asia Minor and Trans-

* Section II will appear in the November, 1936, issue, and Section III, with a list of references relating to Sections I–III, in the December, 1936, issue.

caucasia. During the present century attention has largely been focussed upon pellagra in the more southern areas of the United States. As far back as 1864 GRAY of New York published an account of a single case. Then in 1902 H. F. HARRIS put on record a case associated with ankylostomiasis. In 1907 six authors wrote upon pellagra in U.S.A., two years later in 1909 one hundred and fifty papers appeared on the subject and since then a vast literature has accumulated upon the disease.

To give some idea of the proportions this endemic may reach a few figures may be given. In the Province of Lombardy with a population of nearly one and a half millions, settled in 1,253 communes, there were in 1830 over 20,000 cases of pellagra, in some areas 3·5 per cent. of the population being affected. In 1881 among sixteen and a half millions total population of affected provinces there were over 100,000 pellagrins.

It was estimated by C. H. LAVINDER that between 1907 and 1912 there were 30,000 cases of pellagra in U.S.A. with a 30 per cent. mortality. In 1916 it was stated that there were in the southern states 150,000 cases with between ten and fifteen thousand deaths.

F. L. HOFFMAN (1933) gives the number of deaths from pellagra in the 5-year period ending 1932 as 30,000.

In Rumania, in 1918, the number of cases of pellagra was estimated at 70,000.

In Transcaucasia with a total population of 1,300,000 E. G. NAUCK (1933) estimated the number of cases of pellagra at between thirty and fifty thousand, the proportion of females to males being as 3 : 1.

It is interesting to note that though all these great endemics have been associated with maize as the chief article of diet, no endemic pellagra has been signalled from tropical countries, leaving out for the moment Egypt, even in those in which maize is the staple article of food.

When sporadic cases of pellagra were first discovered in France many authorities refused to acknowledge them as true pellagra and the same failure to realize sporadic pellagra persists to-day. In any case it may be a disease difficult of recognition unless the possibility be borne in mind. Unquestionably many cases all the world over pass unrecognized and die undiagnosed. With interest once awakened, pellagra will often be found if searched for, where previously unsuspected, as well exemplified by T. E. H. THAYSEN (1933) and others in Denmark.

With this brief reference to pellagra in temperate countries it is interesting on turning to warm countries and the tropics to find how rarely the disease has been observed, if we can judge by published reports.

In the following pages, although it cannot be considered to be exhaustive, some attempt has been made to collect together our knowledge of the geographical distribution of the disease.

AFRICA.—To F. PRUNER (1847) is usually ascribed the first description of cases of pellagra in Egypt though Billod at the time was disinclined to accept them as such.

Under the heading of "Leprosies" PRUNER said "Pellagra is sporadic in Egypt and such as we have studied it in Milan. We have seen three cases among the peasants one of whom presents to-day, twelve years after our first seeing him, paresis of the upper limbs, with retraction and muscular atrophy."

A. FIGARI (1865) wrote of a " venereal disease " in Lower Egypt exhibiting " a kind of Leprous Pellagra." HAMEAU's son recognized pellagra in a soldier returned from Algeria in the Hospital of St. André, Bordeaux, in 1850. DE BUCHERIE saw cases among the inhabitants of the Bu-Mezug Valley and among the inmates of the prisons at Ain and Bey. He thought that the first cases of pellagra to be recognized in Tunisia were those noted by ABEILLE in 1851 among Arabs, near Calle between Bône and Tunis. An account of pellagra in Algeria was published by J. de PIETRA SANTA (1880). In 1891 Surg. Capt. AYLES (cited by Sandwith) saw four cases of pellagra among 6,000 starving Arabs at Tokar on the Red Sea Coast.

Pellagra in Egypt is usually associated with the name of F. M. SANDWITH ; writing in the British Journal of Dermatology (1898) he gave an account of his discovery of the disease in Egypt in 1893 and of subsequently seeing 500 cases among the maize-eating fellaheen. It is unnecessary to make further reference here to the disease in Egypt, the facts are well known.

It is stated that SANDWITH saw one or two cases of pellagra among the inmates of the leper colony on Robben Island ; this statement is repeated by DRUMMOND but denied by CULVER (*vide infra*). With this doubtful exception and possibly a case from West Africa, referred to by SAMBON in a private letter, pellagra had never been recorded in Africa except from the Mediterranean area until H. S. STANNUS described in 1911 (1912) an outbreak which he had had under observation during the previous year among the inmates of the Central Prison at Zomba, Nyasaland. Two years later in a second communication, STANNUS (1913) gave a fairly full account of the disease and established the fact that a maize diet was not an essential factor in the aetiology of pellagra.

Soon after these earlier observations upon pellagra in African natives, P. A. NIGHTINGALE published (1912) an account of an outbreak of what he called " Zeism," to distinguish it from pellagra, among the inmates of the Victoria Gaol, Northern Rhodesia. Some 40 cases occurred among men whose main article of diet had been changed from " rapoko " (eleusin) to steam-milled mealie meal. When a return was made to the previous dietary the cases recovered and it was stated that no recurrence took place the next season.

NIGHTINGALE described the typical rash of pellagra, the typical affection of the tongue and lips, etc., but in ignorance of that disease he failed to recognize pellagra though others who read his account, including SAMBON (1913), immediately did so. NIGHTINGALE made a second communication two years later (1914).

J. DRUMMOND (1913) published the case of a tuberculous kaffir, admitted to the Addington Hospital, Durban, suffering from pellagrous rash and tongue, spasmodic diarrhoea, and albuminuria, emaciation, marked inco-ordination, loss of reflexes accompanied by delusions.

He mentioned that Dr. ADDISON had told him that he had seen numerous cases among rebel Zulu prisoners in the 1906 Natal rebellion. E. H. CLUVER (*vide infra*) refers to a communication from Dr. L. G. HAYDON, who put the number of cases at 150. Dr. KNIGHT also stated that he had seen cases in 1907 which closely conformed to the description of pellagra, in the Tugela Valley, they all died.

In 1912–13 an outbreak of pellagra occurred among the inmates of a mental institution at Pretoria, but an account of the outbreak did not appear until the publication of the Annual Health Report, Union of South Africa, June 1928. There were 60 patients, 15 of whom died :

skin manifestations and diarrhoea were the most prominent symptoms, together with " neuritis " of very variable severity. Three cases were reported, but not all published, by BARCROFT-ANDERSON, in East London gaol in 1913, 1914 and 1915 ; they are referred to by CLUVER (*vide infra*).

The case reported by J. A. MITCHELL (1914), a Transkei native transferred from East London prison to Capetown gaol with hemiplegia, rhinitis and scaly anaesthetic patches of dermatitis on the face, back, buttocks, forearms and legs, oedema of feet, spongy gums and tachycardia may have been a case of pellagra but it is much more suggestive of leprosy, in spite of a negative nasal swab.

E. W. D. SWIFT & H. E. BROWN, writing in 1914, stated that Dr. MACFARLANE remembered seeing five cases presenting symptoms of pellagra among the Basuto in 1906–7, and that in the Bloemfontein Asylum six cases were called to mind as having had signs of the disease during the eight years ended 1914.

These authors very truly remark " In Africa, therefore, ability to recognize the disease has played a large part in extending our knowledge of geographical distribution."

This phrase would have been even more true had it been stated conversely.

In 1920 DRUMMOND recognized another case of pellagra in DURBAN. He made enquiries throughout the Union of South Africa but could hear of no other case at that time. He saw yet a further case in 1922. These were the first Europeans to be so diagnosed in South Africa. But the same year PIJPER (1922) reported having seen two similar European cases on the Witwatersrand. He remarks that although maize is the staple diet of a large proportion of natives in South Africa, pellagra is unknown.

A. J. ORENSTEIN, in an investigation among miners on the Rand in 1927, discovered one European and one native case. The same year ROSS & RHODES made a diagnosis of pellagra in an Amatikulu native supposed to be suffering from leprosy, and three native cases were reported from the Addington Hospital, Durban.

In 1928 seven further native cases were diagnosed in the Addington Hospital, one was reported in the Krugersdorp gaol and one in the Queenstown municipal location in reply to a questionary sent to twenty-one District Surgeons attending prisons. These various cases are mentioned by E. H. CLUVER (1929), who further reports upon the outbreak of Pellagra in the Durban Prison Command when 64 cases came under observation : two had symptoms on admission ; 25 within three months of admission ; 10 in between one and two years ; 13 in upwards of two years. The diet, which was deficient in protein, fat and carbohydrate, consisted of mealie-meal, rice, meat or beans, vegetable curry, bread and soup. CLUVER asks why did pellagra break out in this Durban prison and not in other prisons under similar conditions and finds no answer, except to say that " exposure to sunlight (Durban is in the subtropics) is known to be a contributory cause of pellagra, especially when associated with hard work."

It is pointed out that natives living on a diet which might well be considered as prescorbutic only develop scurvy when given the same diet in prison and it seems probable that the same is often true of natives who come into the gaols in a sub-pellagrous state. Unfortunately, the symptomatology in this outbreak is not dealt with and nothing further can be said about it.

In 1924 T. D. NAIR reported the case of a 35-year old Indian in Kenya suffering from recurring attacks over three years of a pellagrous-like rash, increasing in severity, associated with soreness of the tongue, intolerance of light, burning sensations, weakness, vertigo and irritability, and pain in the back and legs.

The same year F. H. COOKE (1924) published a short note upon a case in the convict prison at Accra, Gold Coast, a male aged 30, convicted nine months before. Five months later he was treated for diarrhoea and indigestion followed by burning and tingling in hands and feet; the diarrhoea returned, he lost appetite and became emaciated. Later still the dermatitis appeared on the dorsa of the hands and feet, forearms and face, and pains in the back and head were complained of. The man was a clerk in a European firm and could afford to live well. Nothing is said of the after history and no mention is made of the prison diet. No other cases were noted at the time.

In 1928 A. J. BOASE refers to 10 cases of pellagra discovered among native prisoners at Lira in Uganda, associated in two cases with xerophthalmia. As a result the malady was sought for in other prisoners in Uganda; 17 cases were found at Kampala and seven at Entebbe. The outbreak occurred, it was considered, as the result of the prison diet which consisted almost entirely of maize and beans, vegetables having been cut off the previous year.

The symptoms were typical and resembled those described by STANNUS—rash, sore tongue and soreness at the angles of the lips (here described as leucoplakia) seborrhoea about the nose, diarrhoea and psychosis. Pricking and burning of the feet were complained of.

After the restoration of vegetables, and the addition of meat to the diet, pellagra, it is stated, was banished.

The disease had not been previously recognized in Uganda but it is worthy of note that in 1924 J. P. MITCHEL had signalled an outbreak of what was called a scurvy-like condition, with oedema and watery diarrhoea, among prisoners at Luzira and Kampala which cleared up when meat and vegetables were added to the diet. A similar outbreak had also occurred in 1919 at Mbale prison.

A. MCKENZIE (1930) refers to the fact that in Tanganyika Territory one case only of pellagra had been recorded in the ten years 1919–28 and then reports four cases from the Songea district jail where the average number of inmates was seventeen, whose diet consisted of whole maize 2 lb., beans 5 oz., oil or ghee ½ oz., salt ¼ oz. Little is said of symptoms but it was considered that they responded to the addition of meat, yeast and spinach to the dietary. The patients had been in the prison one, two, one and five months respectively.

In 1933 Dr. Cecily WILLIAMS gave an account of a very interesting condition met with at Accra on the Gold Coast under the heading "A nutritional disease of childhood associated with a maize diet." The syndrome, to use her own words, consisted of "oedema, chiefly of the hands and feet, followed by wasting, diarrhoea, irritability, sores chiefly of the mucous membranes and desquamation of areas of skin," and was due, it was believed, to an improper diet containing an excess of maize. Such a group of symptoms is certainly suggestive of pellagra and when the symptomatology described is studied in greater detail, a diagnosis of pellagra would seem to be inevitable. Miss WILLIAMS, however, came to exactly the opposite conclusion and gave a number of points in differential diagnosis from pellagra. Each of these points

was, however, based upon a lack of appreciation of the symptomatology of that disease as pointed out by STANNUS (1934). In 1935, however, Miss WILLIAMS under the title " Kwashiorkor " published a second article covering practically the same ground and repeating the same errors, an article which drew from STANNUS (1935) even more severe criticism.

These children presented some oedema of the extremities, a typical pellagrous dermatitis of areas of skin subject to trauma, with hyperpigmentation and desquamation ; the extensor surfaces about the knees, ankles, wrists and elbows were affected, and sometimes the thighs and buttocks. Stomatitis and vaginitis were noted and the angles of the mouth and eyes were involved. Diarrhoea and mental irritability completed the picture of pellagra. Ninety per cent. of the children died.

It is worthy of note, however, that among some of the older children, who recovered, relapse occurred. The condition had been seen mostly in children between the ages of six months and four years—nine weeks and five years being the extremes of age in these cases. They had been ill-fed and given a gruel made from partially fermented white maize. Malaria, bronchitis and helminth infections were commonly present. A trace of albumen was found in the urine of some cases but there was no anaemia.

These are, I think one may say, obviously cases of pellagra in children.

In 1935 N. A. Dyce SHARP described a case which he recognized as similar to that portrayed by Dr. WILLIAMS but he also failed to realize the close similarity or identity with pellagra and believed the condition " constitutes a disease *sui generis* " and that there was no evidence of an avitaminosis. In his case there were mental irritability, oedema of hands and feet, enteritis, dermatitis above the wrists and ankles, on the knees, ankles and buttocks—all areas of pressure as he points out, while failing to recognize that this occurs typically in pellagra. There was also stomatitis but no anaemia, and no albuminuria ; the reflexes were normal.

J. F. CARMAN (1935) in a letter referring to the cases described by Miss WILLIAMS and by Dyce SHARP states that a similar affection occurs in Kenya among the Kikuyu children aged 1 to 4 years. The symptoms are oedema of the feet and legs, hands and arms, or whole body including the face, associated with bronzing of the skin and patchy desquamation ; diarrhoea is inconstant, albuminuria not present ; all the children so affected died. He refers to the first case shown by Dr. SHAW at Nairobi and to those observed by R. U. GILLAN (1934–35) and by D. V. LATHAM (1935). GILLAN's cases were mostly breast fed Kikuyu children 3–4 years of age but several cases had been seen among adult females. The outstanding feature was marked oedema extending to the whole body which pitted on pressure.

There was a history of diarrhoea in most cases and the symptoms in some had been present for seven to nine months ; in three of the twelve there was marked tachycardia, in one enlargement of the heart ; pain on movement of the legs was marked, a considerable degree of anaemia was noted but stomatitis was not seen. The condition was considered by the author to be an infective one. While it is difficult to offer any very definite opinion upon the nature of these few cases, the condition would appear to be more closely allied to child beriberi ; it does not resemble very closely that described by Miss WILLIAMS. A somewhat similar single case has been recorded by A. SWARBRECK (1932). A girl,

8 years of age, met with near the southern border of Abyssinia, exhibiting anasarca, ascites, albuminuria and anaemia, a dry scaly skin with purpuric areas, spongy bleeding gums, and dilated heart, which responded to a diet of vegetables, fruit, eggs, milk and meat. The natives recognized the sickness as one usually occurring in outbreaks and then invariably fatal. The author considered the case to be one of scurvy. The ordinary diet of these natives consisted of cows' milk, the pasturage being very poor.

Further references will be made later to the outbreak of pellagra described by STANNUS, also to pellagra among the Turkish prisoners of war in Egypt, described by BIGGAM and to the pellagra recorded by CORKILL among Sudanese millet eaters.

Search through the Annual Medical Reports of our African Colonies yields the following information in regard to cases of pellagra diagnosed: Gambia (1933) 10; Kenya (1932) 2; Nyasaland (1932) 88 in prison, 8 in Asylum, 5 in Hospital; (1933) 10; N. Rhodesia (1932) 12 in Broken Hill Gaol; (1933) 6; Zanzibar (1933) 16; Basutoland (1933) 3; Bechuanaland (1933) 1; Swaziland (1931), a pellagra-like condition is noted.

Pellagra is not mentioned in the reports for Lagos, Sierra Leone (1932), Nigeria (1932), Tanganyika (1932), Somaliland (1928), Mauritius (1932), Seychelles (1931).

One would not be surprised, however, if these figures were found to give a completely erroneous picture of the distribution of pellagra.

INDIA.—J. C. D. MEGAW & J. C. GUPTA (1927), in an article upon the geographical distribution of some diseases in India, basing their opinion on the replies made to a questionary sent to civil surgeons, say of pellagra there are only four doubtful cases from Lyallpur and one well-authenticated case from Calcutta by Col. CALVERT and one other possible case at Natore from Col. SANDES. It is interesting to note that in a later paper MEGAW (1936) gives the figure for cases of night-blindness in India at three and two-thirds millions, more than twice the number of cases of pulmonary tuberculosis. The figures given by MEGAW & GUPTA most assuredly give no idea of the incidence of pellagra in India. The probability is that when pellagra is unsuspected and when there are few able to recognize the disease, many cases go undiagnosed.

A. SWARUP (1930) has described a typical case of pellagra from Ballia, United Provinces. The patient was a non-maize eater and rarely partook of meat or fish. The typical affection of the skin was associated with pyorrhoea, stomatitis, erosions at the angles of the mouth, tremor of tongue, giddiness, sleeplessness, "pins and needles" in the hands and feet, exaggerated knee-jerks, and diarrhoea with a seasonal variation in symptoms.

In 1931 and again in 1933 J. LOWE has described an outbreak of pellagra among the inmates of the Leprosy Hospital at Dichpali, Hyderabad, Deccan. The disease was first noted in 1925. Twenty cases were diagnosed in the next six years, eleven women and nine men, though the proportion of female inmates to male was as 1 : 4. The ages were from 14 to 40 years. In 1931 twenty fresh cases occurred.

The skin manifestations, etc., were typical including the affection of the genitals and stomatitis in 50 per cent., but, except in seven cases, intestinal disturbances with diarrhoea were uncommon. In the same way nervous and mental symptoms though typical, were not common. Signs appeared in December, reached a maximum in March, and then cleared in April.

Fatal termination was associated with myocardial failure—tachycardia, dyspnoea and oedema of the feet. The diet provided by the Mission which looks after the Leper Hospital consisted of 1 lb. unmilled rice, a chapati of jawari (millet) flour, salt, ghee and one anna a day to purchase dhal, meat, fish or vegetable, if any available.

LOWE thinks that though such a diet shows a marked deficiency in protein and an excess of starch, it is much the same as that taken by the population outside the institution and believes that this points to some infection as the cause of pellagra.

T. K. RAMAN (1933) has published notes of four typical cases of pellagra at Guntar and remarks that no cases had been previously reported in the Madras Presidency.

B. H. RAJADHYAKSHA (1933) similarly notices a case in Bombay.

S. N. GUPTA (1935) a case at Lahore—female aged 20, who had lived on wheat, fruit, vegetables and ghee. The rash appeared on the hands, feet, forearms, legs, elbows, nose, cheeks and neck ; the skin was dry and thickened. Diarrhoea, mental depression and marked anaemia completed the picture.

G. PANJA (1935) also cites a case in Calcutta, and N. S. H. MODY (1935) one at Poona very similar to that described by GUPTA.

CEYLON.—Pellagra is said not to occur in Ceylon. L. NICHOLLS (1934), who gained acquaintance with the disease in the West Indies stated that he had searched for cases of pellagra in the Ceylon prisons, vagrant asylums, poorhouses, etc., in vain.

RUSSIAN TURKESTAN.—A. J. WYJASNOWSKY (1934) mentions twenty cases of pellagra seen at the Psychiatric Hospital, Tashkent, of whom more than half died. In the same city J. KASSIRSKY & L. BUROVA (1932) have had under their care, in the clinic for Tropical Diseases, forty-eight cases of pellagra. There was a mortality of 28 per cent. and of those who improved with better diet 30 per cent. relapsed the following spring.

CHINA.—S. R. ROBERTS (1912) quotes W. H. JEFFERYS as replying to a letter of enquiry to the effect that pellagra had never been reported from that country. He very wisely adds that this does not mean that the disease may not be present as he has been misled so often, and further, " I do not think that the average surgeon or physician would recognise pellagra unless on the lookout for it, or unless its great prevalence as a disease should force his attention." The first cases actually to be reported were four in number from Szechwan, Western China, by H. JOUVEAU-DUBREUIL (1919).

Since then a number of observations have been published and it may be of interest to summarize here some of the findings in regard to the disease as seen in the Far East. E. S. TYAU (1923) makes the interesting observation that among some 6,000 cases that had passed through the skin clinic at St. Luke's Hospital, Shanghai, in the previous eight years none has ever been suspected of pellagra, but that in the next year six cases had been recognized. All were males over forty years of age belonging to the poor working class, living on rice. " The skin of the backs of the hands, and of the cheeks was dry, thickened, rough and darkly pigmented." The tongue was dry and painful with reddened edges ; there were aphthous ulcers on the fauces, loss of appetite, abdominal pain and diarrhoea ; " burning sensations " in the soles of the feet and later nervous symptoms and fatal termination.

S. C. Wu (1923) refers to the first case ever observed at Wuhu ; a male, 36 years of age, boatman. His illness began with " burning sensations " in both hands, followed by dermatitis of the backs of the hands and round the wrists and both feet, and later desquamation. There were also affection of the tongue and lips, loss of appetite, abdominal discomfort and diarrhoea ; numbness over the upper and lower extremities and chest, and lost reflexes. His diet consisted chiefly of rice, vegetables and only occasionally fish, never meat.

Mu Jui-Wu (1927) of Peiping, relates the case of a soldier, one and the only one of a party of ninety to develop the disease. They all partook of the same diet of rice, cabbage, bean-cure, bean-sprouts, spinach and turnip but seven months before being seen the patient had changed the diet to one consisting of millet and after two months maize with turnip, cabbage and spinach. His chief symptom was an intolerable " creeping sensation " in the legs with weakness. The dermatitis affected the hands, wrists, fore-arms and neck ; the tongue was glossy but there was no stomatitis ; a seborrhoeic affection of the skin of the face was noted. Symptoms cleared up when given a full diet and hydrochloric acid. Seven other similar cases were recognized later.

A. C. Lambert (1927) has published a case of pellagra in a Chinese woman at Honan suffering from a recto-vaginal fistula who had lived on wheat-meal and vegetables only. She presented the typical affection of the skin and tongue, associated with diarrhoea and nervous symptoms.

C. S. Yang & C. K. Hu (1930) have described three interesting cases at Peiping. The first was a male aged 42, complaining of twelve months diarrhoea following an attack of dysentery, progressive weakness and numbness of the lower limbs. Examination revealed a palpable spleen, absent knee-jerks, marked anaemia, red cells two millions, and haemoglobin 32 per cent., hypochlorhydria, a normal urine, extensive ulceration and polyposis of the rectum, a pellagrous rash on the hands, nose and cheeks of six months standing, and a fissured tongue ; the stool was negative for *Bact. dysenteriæ*. The diet had consisted practically entirely of cereals. When he was placed on a full diet the skin lesions disappeared and the haemoglobin rose to 82 per cent. The second case was a 14-year old servant girl the subject of pulmonary tuberculosis who had existed on a diet of cereals and vegetables. A typical rash on the backs of the hands was associated with diarrhoea. At the time she was seen the skin was still sensitive, as a small dose of U-V radiation on the abdomen caused an erythema to appear. The third case was a 24-year old male who had had chronic diarrhoea for over three years and had lived on cereals, green and salted vegetables. For eight months a pellagrous eruption had been present on the backs of the hands, forearms, back of the neck, face and sternum. There were also loss of weight and diminution of patellar response, but no anaemia and no other symptoms ; amoeba, ascaris and monilia infections present. Treatment with emetine, E.B.I., yatren, hydrochloric acid and a full diet was instituted and the skin lesions almost disappeared but the patient died a few days later, extensive ulceration of the bowel being found at necropsy.

C. S. Yang & K. K. Huang (1934) describe 30 cases of pellagra among soldiers in an army camp at Nanking. The eruption was typically on the hands ; in 27 the mouth or tongue was affected, the tongue raw and the papillae red and swollen. Associated symptoms consisted of giddiness and irritability but no frank mental symptoms, numbness

and weakness of the lower extremities, pain in the calves on pressure ; loss of muscle tonus and oedema in a few ; variable knee-jerk ; scalding, darting pains and pins and needles in the soles of feet. Blurring of vision with reduced fields and night-blindness occurred in 25. In one case retrobulbar neuritis was noted. A " folliculitis " was present on the anterior part of the trunk. Diarrhoea was not present but there was often a history of it. Rectal examination revealed in a number of cases a proctitis. It was noteworthy that 29 of the 30 cases occurred in a cavalry camp and only one in the artillery camp. The diet was rice 200 catties, wheat flour 150, turnip 52, green cabbage 7, green bean 10, vegetable oil 4, pork 3, *i.e.*, low in protein and high in carbohydrate.

K. Y. Yu (1934) describes the first three cases of pellagra in Manchuria. Typical rash was associated with raw and furred tongue, wasting, vulvitis and soreness at angles of mouth and about the anus, dizziness, epigastric pain, pyrosis, diarrhoea, pain in the back, diminished knee-jerk, some oedema of legs and mental depression. The diet consisted of practically nothing beyond millet, with or without salted vegetables and bean-sprouts. In one case there was active pulmonary tuberculosis.

KOREA.—R. M. WILSON (1925 and 1933) gives an interesting account of an outbreak of pellagra in Leper Asylums in Korea, he being unaware that the disease had been ever reported before from Korea or China, and certain that he had never seen the disease in the previous seventeen years. In 1925 lepers in the Kuangju Colony, with 600 inmates, began to complain of a brown, scaly, exfoliative rash on the arms and legs, like an iodine burn, which disappeared in the winter, to reappear in the spring. The relative frequency of symptoms was : scaly skin 17 ; erythema 15 ; stomatitis, sore gums and red tongue 15 ; nausea and vomiting 15 ; gastro-intestinal upsets 12 ; bloody stools 8 ; salivation 9 ; headache 13. Referring to the colony at Fusan in 1933 Wilson says " the red disease " has become very common both there and at Soonchun.

The exanthema was typical, affecting hands, neck, ankles, face, etc., associated at first with constipation and then with diarrhoea ; nervous symptoms were not marked and in only three was there insanity. In all there were six males and 30 females affected, some died but the number of deaths was not recorded. Relapses up to seven years had been noted. A questionary was sent to other Mission doctors in Korea: nine had not recognized pellagra, three had done so. K.S. OK of SEOUL had records showing two cases of true pellagra, and 19 cases of pellagroid [*sic*] in twelve years, otherwise the disease had not been seen outside institutions, though, it is stated, a pellagra-like condition had been observed among chronic alcoholics and in some suffering from " tuberculosis or other chronic illnesses in which diet and food absorption were at fault." Such cases are, of course, in reality pellagra.

The diet of these leper cases was a poor one, consisting of rice, vegetables, some beans and barley. It is rather remarkable that cases were said to improve when pork or codliver oil was added to the diet. Probably the rash would have improved in any case.

JAPAN.—M. ITOH (1925) refers to pellagra in Japan. He has collected references to sixty cases and himself has seen twelve ; cases were found on the main island, in Korea and Formosa, practically none in the north island. They occurred among ill-nourished workmen

living on a polished rice diet and were cured by giving rice husk. Of the sixty, 27 had diarrhoea, 18 stomatitis and indicanuria, 8 psychosis; many had signs of a peripheral neuritis, in 19 resembling beriberi.

S. Takahashi *et al.* (1929) state, that over seventy cases of pellagra have been recorded in Japan. They give an account of four fresh cases seen at Hokkaido; three females aged 41, 45 and 54 and one male aged 43. They were typical cases with a history of gastro-intestinal disturbance. In one woman carcinoma of the pylorus was present.

Philippine Islands.—J. N. Rodriguez (1930) has published a case of pellagra from the Philippine Islands, and refers to one observed by D. D. Willets in 1910. The patient was a maize eater, a moderate taker of "tuba" but seldom got meat, chicken, or eggs and never milk. The illness began with pain and diarrhoea and the passage of tarry stools. He became very weak and thin, and developed an exanthem on the hands, forearms, nose, forehead and cheeks, with "burning sensations" and what is called a "prickly" seborrhoea. The tongue was sore and red at the tip and borders. Later the man became liable to depression or excitability.

T. Dychitan (1930) describes a condition called "Lapnus," a common affection in the island of Mindoro Philippines, which he thinks is pellagra.

It prevails from March to August, and disappears in September and has a mortality of 50 to 60 per cent. "Burning of the soles of the feet" is a prominent symptom followed by the development of a purplish-blue colour, later on a gray colour, and cornification then peeling of the skin. Other symptoms are stomatitis, gastralgia and pyrosis; pains in bones, formication in, and weakness of the lower limbs, increased knee-jerk, mental apathy and melancholia. Opacity of the cornea sometimes occurred. One would agree, obviously pellagra.

Siam.—R. W. Mendelson (1919 and 1923) writing of Siam believed that no cases of beriberi or pellagra had been reported from that country. He then describes a police recruit aged 27 suffering from a raw red tongue, dermatitis affecting the dorsa of the hands and feet and scrotum, associated with diarrhoea, the gait of polyneuritis, diminished knee-jerk but no oedema. Mendelson suggests it was a case of mixed pellagra and beriberi but there seems little reason to believe it was anything more than a case of the former.

Malay.—As far as I am aware no outbreak of pellagra has ever been recognized as such in south-eastern Asia and it has sometimes been said that pellagra does not occur. That the disease often goes unrecognized is very probable and borne out by the statement made by W. S. Sheppard of Singapore (1912). Until he had learned to recognize the disease, cases were labelled "a hitherto undescribed form of superficial dermatitis, probably tropical in origin," and one of his colleagues who had practised in the East for twenty years told him he had not infrequently noticed similar skin lesions without recognizing them for what they were, namely pellagra.

Sheppard remarks that during the years 1903 to 1907 he was constantly seeing cases in his wards at Singapore. He also notes that they came from the poorest classes and that they were rice eaters. J. V. Landor & R. A. Pallister (1935) to whose observations reference will be made later, state that sporadic cases of pellagra do occur among the general population of Malay and cite in brief three cases.

A. VISWALINGAM (1917) referred to the first case of pellagra seen by himself in Perak. He made other references to pellagra the next year (1918), at the Sixth Congress Far Eastern Association of Tropical Medicine (1925) and again later (1929). He discusses cases of pellagra occurring among Chinese and Indian labourers.

Attention is called to the characteristic symptom of " burning feet " called in Chinese " pee." The typical rash was associated with stomatitis, raw tongue, soreness at the angles of the mouth, diarrhoea, numbness and weakness in the limbs, oedema, absent knee-jerks and melancholia. He believed that the disease was due to a monotonous diet, deficient in vitamins, poor in protein with excess of carbohydrate, such a diet as the native takes—polished rice, salt dried fish, pork fat, tubers, some fresh or preserved leaves, with stale vinegar as a sauce. His theory is that many patients as the result of malaria, dysentery and ankylostomiasis suffer from defective digestion; prolonged dietetic deficiency leads to an intoxication which causes pellagra.

Returns for pellagra in the Annual Medical Reports are as follows: Strait Settlements (1932) 2; Hong Kong (1932) 24 Chinese; Singapore (1933) no mention; Johore, Kedah, Penang, Kelantan (1932) no mention. Federated Malay States (1933) none.

PAPUA.—W. M. STRONG (1932) mentions a number of cases of keratitis and panophthalmitis with night-blindness and signs suggestive of beriberi and scurvy among natives in a large centre of native employment, but no details are given. It would have been interesting to know if any of these cases resembled more closely pellagra.

DUTCH EAST INDIES.—W. G. BOSCH (1931) reports a single case of pellagra in Java, and C. D. DE LANGEN & B. DJOHAN (1935) a case in Sumatra (Batavia); a typical case in a male native aged 35, with exanthem, glossitis, mental depression, slight oedema of legs and marked anaemia.

SANDWITH cited NEIRET as reporting pellagra in New Caledonia.

AUSTRALIA.—S. J. CANTOR (1927) of Melbourne has published an account of five cases of pellagra in which the diagnosis rested upon a typical rash associated with mental symptoms. In one of the two male cases it is noted that the scrotum was also involved. N. PAUL (1928) of Sydney also reports a case of the disease, a man aged 46 who was edentulous and had lived for years on farinaceous foods and beer. He suffered from flatulence, dyspepsia and constipation, mental irritability, nervousness and depression, weakness and vertigo, soreness at the angles of the mouth, an ulcer on each eye, and a characteristic dermatitis on the hands, forearms, face and neck, which had recurred each summer for five or six years.

CENTRAL AMERICA.—Pellagra was reported in Mexico by D. NIBBI in 1882. Mortality statistics for Mexico quoted by S. R. ROBERTS (1912) returned one death from pellagra in Mexico City in 1909 and one in Monterey City in 1910. R. ROMERO (1931) states that the disease is common among the half-breeds of the province of Yucatan, who subsist on a deficient nourishment, together with alcohol. At Merida with a population of 80,000 the deaths from pellagra have been: 1911, 49; 1912, 71; 1913, 22; 1914, 81; 1915, 70; 1916, 91; 1917, 72; 1918, 29; 1919, 23; 1920, 21. GAUMER went so far as to say that 8 to 10 per cent. of the population was affected.

J. L. PHILLIPS also cited by ROBERTS refers to pellagra in the Panama Canal Zone and says that in the years 1909–11 32 cases had been diagnosed with 16 deaths.

Of the incidence of pellagra in South America little is known.

WEST INDIES.—The Annual Medical Reports make returns as follows: Trinidad & Tobago (1933) 1; St. Christopher & Nevis (1932) 1; St. Lucia (1933) 2; St. Vincent (1933) 0; Antigua (1933) 2; Dominica (1933) 0; Jamaica (1932), a few deaths from pellagra occurred; Bermuda (1932) 0; Barbados (1932–3) 100; Virgin Islands (1933) 0. British Honduras (1933) 1; British Guiana (1932) 0, may also be mentioned here.

In the 1932 Report for Bahamas the following figures are given for the years 1928 to 1932; 35, 86, 79, 81, 61, 35 and 27 cases of pellagra. It is stated that pellagra is always more obvious when the citrus fruit crop fails owing to hurricane.

VELARDE (1932) saw five case of pellagra among 475 admissions to hospital in twelve months 1931–32 in the Island of Porto Rico.

It is interesting to remember that pellagra in Barbados was first described by C. G. MANNING in 1909 among the inmates of the asylum under the name of "Psilosis pigmentosa." The symptoms recounted consisted of a scurfy crusted skin over the points of the knuckles, elbows, knees and feet (except in those who wore shoes) more rarely on the back and chest, accompanied by anorexia, stripping of the mucous membrane of the tongue, cheeks and fauces, intractable diarrhoea and anaemia. The skin took on a "wine stained" tint and gangrene sometimes occurred. The patients became "silly and half-witted" but with good feeding, milk and cod-liver oil recovery took place.

Pellagra was first recognized in Jamaica in 1897 according to D. J. WILLIAMS. In 1905 4 per cent. of the total 1,050 inmates of the Asylum "were attacked with Pellagra in our wards." For twelve months no maize foods were allowed into the asylum but persons admitted during that time still got the disease.

RABIES.

A REVIEW OF RECENT ARTICLES. XXV.*

The rôle of the vampire bat in the transmission of rabies in Trinidad and in parts of South America is the subject of four papers. The first by PAWAN, the second by DE VERTEUIL & URICH, and the third by METIVIER refer mainly to Trinidad; the fourth by TORRES & LIMA is from South America. In all four papers the conclusion is arrived at that the vampire bat is the transmitting agent in these epidemics and epizootics.

PAWAN[1] first fixed his attention on the examination of bats which showed unusual behaviour, and tested these for rabies both histologically and by animal experiment. It is difficult to extract the exact figures from the paper, but it may be said that in practically all of the bats examined (roughly 38) there was definite evidence of the presence of rabies virus. Crossed immunity tests were then carried out with fixed virus and bat virus, with the result that fixed virus protected against bat virus, but bat virus protected only feebly against fixed virus. It was also found that fixed virus antiserum neutralized bat virus. The author then gives details of forty-seven cases of rabies, in all except one of which there was a history of bat bite, and draws attention to the fact that in all except one, sensory symptoms at the seat of the bite preceded paralysis and death. He then deals with preventive measures, such as bat-proofing of stables and dwelling houses, and describes the mode of attack of the bat. Finally he draws attention to the comparative rarity of canine rabies in Trinidad, as well as in Brazil. Whether this can be explained by assuming, (1) that the local virus is innocuous to canines, or (2) that dogs are never bitten in their sleep, or (3) that the dogs of these countries possess an immunity, he is not prepared to say.

DE VERTEUIL & URICH[2] cover somewhat similar ground. The latter is responsible for the zoological side of the investigation, and the former for the bionomics of the vampire bat (*Desmodus rufus*). They refer to the epizootics of paralytic rabies reported from Santa Catharina in Brazil since 1906, the transmitter of which was believed by HAUPT & REHAAG (1921) to be the vampire bat, *Desmodus rotundus*, and briefly describe the experience in Trinidad and its experimental elucidation by HURST & PAWAN. The characteristics and life history of *Desmodus rufus* are then described, with very interesting illustrations. It appears that the bat grasps the victim by the canine teeth, and with its sharp triangular upper incisors cuts through the skin; the blood is then lapped up, the tongue moving forwards and backwards like a piston. The bats may be destroyed in their feeding grounds, in the places where they digest, or in their roosting places. As regards the first locality advantage is taken of the fact that the bats " have the habit of biting

---

* For the twenty-fourth of this series see 1936, Vol. 33, p. 316.

[1] PAWAN (J. L.). The Transmission of Paralytic Rabies in Trinidad by the Vampire Bat (*Desmodus rotundus murinus* Wagner, 1840).—*Ann. Trop. Med. & Parasit.* 1936. Apr. 8. Vol. 30. No. 1. pp. 101–130. With 2 maps & 4 figs. on 1 plate. [56 refs.]

[2] DE VERTEUIL (Eric) & URICH (F. W.). The Study and Control of Paralytic Rabies transmitted by Bats in Trinidad, British West Indies.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Jan. 25. Vol. 29. No. 4. pp. 317–347. With 20 figs.

the same animals on the same spots nightly." Strychnine paste is applied to this area, and the bats are poisoned with ease. Trapping or fumigation is used in the digesting and the roosting places. The authors then describe experimental work which has been carried out both in Trinidad and in Brazil. Most of this has already been described in these reviews. But one observation emanating from Brazil is worthy of note : " Four desmodus bats after inoculation with bovine rabies virus, though showing no symptoms of rabies themselves, were capable of transmitting the infection to twenty-five healthy cattle within one to four months after experimental inoculation. One such bat, killed after five months, was proved to have its salivary gland infected." The authors rightly conclude that " Confirmation of this last experiment would mean not only a new addition to our knowledge of the virus of rabies, but would also further indicate the necessity for considering the carrier problem in connection with viruses in general." Usually, however, the bat dies after a period of a few days during which it has shown a " change of habit " and has appeared to be restlessly active. The authors believe that the disease is also transmitted from bat to bat, basing this conclusion on the occurrence of scars on the heads and bodies of captured bats, and upon the fact that when hungry they commonly attack each other. The enzootic may be controlled by bat destruction as described above, and for this, surveys of infected areas and of roosting places, of which illustrations and maps are given, are necessary. " The possible relation of fruit eating and other bats to the spread of the disease appears to require further investigation."

The paper by METIVIER[3] covers similar ground, and deals with the veterinary aspects of the problem.

The observations made in Brazil are described *in extenso* by TORRES & LIMA,[4] and a French summary of this paper appears in another journal.[5] The larger paper is furnished with beautiful illustrations of the vampire bat and with photographs showing the bat as it attacks various animals. An historical account of the cattle epizootics in Brazil and of the work of HAUPT & REHAAG and others is also given. The experiments cover a wide range, and show that the vampire bat is without doubt the transmitter of the epizootics in question, the resulting disease being rabies of paralytic type.

i. *Virus.*

The size of the virus of rabies (fixed virus) has been examined by YAOI, KANAZAWA & SATO,[6] using the technique devised by ELFORD. The brain of a rabbit killed in an advanced stage of rabies was ground with sand in a mortar, and suspended in a suitable diluent (Hartley's

[3] METIVIER (H. V. M.). Paralytic Rabies in Livestock.—*Jl. Comp. Path. & Therap.* 1935. Dec. 31. Vol. 48. No. 4. pp. 245–260. With 7 figs. [11 refs.]

[4] TORRES (Sylvio) & LIMA (Esperidião de Queiroz). A raiva e sua transmissão por morcegos hematophagos infectados naturalmente.—*Rev. Depart. Nac. da Producção Animal.* Rio de Janeiro. 1935. Vol. 2. Nos. 1, 2 & 3. pp. 1–55. With 25 figs. on 11 plates & 1 folding diagram. [17 refs.] English summary.

[5] TORRES (Sylvio). La rage et sa transmission par les vampires hématophages. —*Rev. Gén. de Méd. Vét.* 1936. Feb. 15. Vol. 45. No. 530. pp. 78–84.

[6] YAOI (H.), KANAZAWA (K.) & SATO (K.). Ultrafiltration Experiments on the Virus of Rabies (Virus Fixe).—*Japanese Jl. Experim. Med.* 1936. Feb. 20. Vol. 14. No. 1. pp. 73–79. [11 refs.]

broth at pH 7·6). The centrifuged suspension, after filtration through sand and pulp, was subjected to filtration through collodion membranes of various grades, under pressure of nitrogen gas. In estimating the infectivity of the filtrates tests were made with ten-fold dilutions of the fluid using guineapigs. The authors found that at a pH of 7·6 the virus passed through membranes with an average pore diameter of not less than 0·2 μ. "We assume therefore the end point of the rabies virus as 0·2 μ, and regard the particle size of the virus as 0·1 to 0·15 μ."

Defries & Campbell[7] find that the New York strain of fixed virus differs slightly from the Paris strain, both in its minimum lethal dose, and in its incubation period when inoculated into rabbits and white mice. The lethal dose of the New York strain is of the order of one in 10^6, whilst that of the Paris strain is one in 10^4. The average incubation of the New York strain in rabbits was 10 days, whilst that of the Paris strain was 15 days. In a further experiment it appeared that subpassage intramuscularly through white mice increased the pathogenicity of the Paris strain.

During the course of experiments on the serotherapy of rabies in mice (this *Bulletin*, 1935, Vol. 32, p. 618) Proca & Jonnesco[8] found that fixed virus recovered from mice which had succumbed after prolonged incubation appeared to be modified. They have examined two such strains in some detail, and find that they are attenuated and differ from ordinary fixed virus in giving rise to a larger number of Negri bodies. This in their opinion is not due solely to the long sojourn of the fixed virus in the tissues of the mouse. The modification appears to be a true mutation.

Bozzelli[9] in continuation of work already reviewed (*ante*, p. 318), on the effects of inoculation of mixtures of fixed and street virus, comes to the conclusion that fixed virus has lost its proclivity for spreading centrifugally or centripetally along the nerve trunks whilst street virus retains this property. On the contrary fixed virus has an increased elective virulence for the central nervous system.

From experiments conducted by Violle & Livon[10] it appears that exposure to 1 per cent. ricinoleate of sodium for 45 minutes at room temperature destroys fixed virus. They now intend to examine the immunizing properties of this killed virus.

Remlinger & Bailly[11] noting this result have tested the effects of the same substance on street virus. The conclusions arrived at from six experiments are identical. "This identity of action does not allow one to envisage the possibility of a rapid and easy method of differential diagnosis between the two viruses (ricino-diagnostic)."

Following their investigation of the effects of low temperatures on rabies virus (this *Bulletin*, 1935, Vol. 32, p. 174) in which it was shown

---

[7] Defries (R. D.) & Campbell (T. C.). The Relative Pathogenicity of Two Strains of Fixed Rabies Virus for White Mice and Rabbits.—*Canadian Public Health Jl.* 1935. Dec. Vol. 26. No. 12. pp. 615–618.

[8] Proca (G.) & Jonnesco (D.). Sur une modification durable du virus rabique de passage.—*C. R. Soc. Biol.* 1935. Vol. 120. No. 40. pp. 1274–1276.

[9] Bozzelli (Roberto). Contributo allo studio delle "settinevriti" da virus rabbico fisso e di strada.—*Boll. Istituto Sieroterap. Milanese.* 1936. Apr. Vol. 15. No. 4. pp. 260–265. [35 refs.] German summary.

[10] Violle (Henri) & Livon (Jean). Action du ricinoléate de sodium sur le virus de la rage.—*C. R. Soc. Biol.* 1936. Vol. 121. No. 2. pp. 100–102.

[11] Remlinger (P.) & Bailly (J.). Action du ricinoléate de sodium sur les virus de la rage et de la maladie d'Aujeszky.—*C. R. Soc. Biol.* 1936. Vol. 122. No. 16. pp. 24–25.

that in frozen condition the virus maintained virulence for at least 600 days and a suggestion by LÉPINE that freezing should be substituted for glycerine in the conservation of cords (*C. R. Acad. Sci.* 1935, Vol. 201, p. 172), REMLINGER & BAILLY[12] point out that much experimentation would be necessary in order to determine how the various properties of the vaccine were affected. These are being carried out at Tangiers.

In the third of a series of articles on Pseudo-rabies (this *Bulletin*, 1934, Vol. 31, p. 146 and 1935, Vol. 32, p. 175) HURST[13] deals with the disease as it occurs in monkeys. The experiments described in the second of the series were performed on rabbits. It will be remembered that in relation to the rabbit the virus was found to be pantropic, *i.e.*, it readily attacks cells derived from any embryonic layer. In the monkey (*Macacus mulatta*), however, it behaves as a strict neurotrope, only nerve and glial cells being affected. Intracerebral, intracisternal inoculation, and in most instances intrasciatic inoculation led to an infection which was usually fatal. No infection in a limited number of experiments followed intradermal, intramuscular or intravenous inoculation. The distribution of the virus after inoculation was carefully followed, and the histological appearances of the various tissues studied. Certain cortical areas—the pyriform area, the cornu ammonis, the island of Reil, the lower lip of the sylvian fissure and the basal surface of the frontal lobe were more affected than other parts of the nerve axis. " The blood and the cerebrospinal fluid play no apparent part in disseminating the virus." It thus appears that the rabbit and the monkey differ markedly in their relation to pseudo-rabies. The author states that the pig and the monkey are possessed of greater resistance than are most common and domestic animals, and points out that in the two groups of animals the mechanism of resistance is wholly different. In the pig " a definite local lesion develops, associated presumably, as in the rabbit, with great multiplication of the virus, only small amounts are necessary to infect by the skin." During the course of infection the virus is present in the blood ; lesions may be found in lymph glands, spleen, etc. The mortality rate is less than 5 per cent. Nasal secretions and urine become infective. " In short, in the pig, the virus exhibits multiple affinities, it easily contracts the disease, but survives because its nervous system is relatively resistant. In the monkey, on the contrary, there is no local reaction ; intramuscular and intravenous inoculation are ineffective ; but if the virus enters nervous tissue, the nervous system may be invaded, and in many instances the issue is a fatal one. The blood is not infected, and the animal is not infective to its cage mate. There are no visceral lesions. In brief, in the monkey the nervous system is probably less resistant to infection than in the pig, but since the virus behaves in this species as a strict neurotrope it does not readily reach the susceptible tissue, destruction of which is incompatible with life."

---

[12] REMLINGER (P.) & BAILLY (J.). La congélation des moelles rabiques est-elle applicable à la pratique de la vaccination ?—*C. R. Soc. Biol.* 1936. Vol. 121. No. 15. pp. 1614–1616.

[13] HURST (E. Weston). Studies on Pseudorabies (Infectious Bulbar Paralysis, Mad Itch). III. The Disease in the Rhesus Monkey, *Macaca mulatta*.—*Jl. Experim. Med.* 1936. Mar. 1. Vol. 63. No. 3. pp. 449–463. With 6 figs. on 2 plates.

The first section of a paper on AUJESZKY's disease by GERLACH and SCHWEINBURG[14] already reviewed (*ante*, p. 320) now appears in another journal. The second section[15] appears in the *Wiener Klinische Wochenschrift*. This deals with the influence of physical and chemical agencies on the virus. It is filterable, passes through Chamberland bougies L_1, L_2 and L_3, but not through Berkefeld V bougies, nor collodion membranes. It is in general rather less resistant to drying and chemical agents than are other viruses. It differs markedly from rabies virus in that on subpassage through guineapigs the incubation period gradually increases until finally the virus becomes avirulent. In twenty instances transference to a cagemate took place without any evidence of wounding. Thus " It is beyond doubt that transference by simple contact can occur." Only exceptionally has infection followed biting. The authors have succeeded in conveying the disease to rabbits by subcutaneous and intra-muscular inoculation by the saliva of a cow suffering from the disease. Crossed immunity tests differentiate the virus from rabies virus.

The occurrence of two cases of AUJESZKY's disease in cattle in France is reported by CRUVEILHIER, TRUCHE & VIALA.[16] These were characterized by sudden onset, and rapid course, shortness of the period of paralysis, and extreme pruritus.

ii. *Symptomatology.*

The case of a man bitten by a dog suffering from " chien fou " which occurred in the Oubangui (West Africa), is described by LE BIHAN.[17] The only unusual symptoms were an absence of deep sensation, and diminution in the tendinous reflexes.

A case of hydrophobia which occurred after treatment, during the course of an attack of malaria is discussed by LÜCK.[18]

DE MELLO[19] describes two cases of rabies, in the first of which the symptoms were those of an ascending paralysis, and in the second the clinical picture was of the usual type.

iii. *Pathology.*

The observation of QUAST (this *Bulletin*, 1926, Vol. 23, p. 693) that after a course of treatment with living fixed virus, the virus may be present in the brain in a latent condition without causing any symptoms of rabies has been the subject of much controversy. Some workers

---

[14] GERLACH (F.) & SCHWEINBURG (F.). Experimentelle Untersuchungen ueber die Aujeszkysche Krankheit (Pseudowut). I. Mitteilung.—*Ztschr. f. Infektionskr. d. Haustiere.* 1935. Vol. 48. No. 4. pp. 270–310. With 17 figs. & 8 charts [51 refs.]

[15] GERLACH (Franz) & SCHWEINBURG (Fritz). Experimentelle Untersuchungen ueber die Aujeszkysche Krankheit (Pseudowut). II. Mitteilung.—*Wien. Klin. Woch.* 1936. May 1. Vol. 49. No. 18. pp. 551–554.

[16] CRUVEILHIER (L.), TRUCHE (C.) & VIALA (C.). Note sur deux cas de maladie d'Aujeszky observés en France.—*Ann. Inst. Pasteur.* 1936. Apr. Vol. 56. No. 4. pp. 395–400.

[17] LE BIHAN (A.). Un cas de rage humaine dans l'Oubangui.—*Ann. de Méd. et de Pharm. Colon.* 1935. Oct.–Nov.–Dec. Vol. 33. No. 4. pp. 1075–1079.

[18] LÜCK (O.). Zur Kasuistik der antirabischen Impfungen.—*Rev. Microbiol., Epidémiol et Parasit.* 1935. Vol. 14. No. 4. [In Russian pp. 417–418. German summary p. 418.]

[19] DE MELLO (A. L. Nobre). Sobre dois casos de raiva humana.—*Folha Med.* 1936. Jan. 5. Vol. 17. No. 1. p. 1.

support QUAST, others have failed to find evidence supporting his contention. It is important for the diagnosis of the type of rabies from which a patient has died, to ascertain whether the presence of a virus, which behaves on subpassage as a fixed virus, is indicative of death from the fixed virus used in the treatment, or whether it is merely the indication of a storage of latent fixed virus in the sense of QUAST.

BUSSON[20] now reports two cases amongst rabbits (previously infected with syphilis), in the brains of which, when the animals were killed twenty-eight and thirty-five days after the completion of treatment by HÖGYES living virus, fixed virus was proved by further passage to be present. These rabbits had shown no symptoms of rabies. A number of other rabbits had been similarly treated, and these gave a negative finding. BUSSON consequently believes that the transmission of fixed virus to the central nervous system as a result of treatment is not a normal occurrence. He is not convinced that the virus found was innocuous. The incubation periods on subpassage were long, and it is possible that the rabbits, though showing no symptoms at the time when they were killed, would have developed rabies later. The conditions under which the fixed virus penetrates into the central nervous system depend in his opinion upon idiosyncrasies in the patient on the one hand, and upon the character of the vaccine on the other.

JONNESCO[21] describes a further case of natural immunity in the dog (this *Bulletin*, 1935, Vol. 32, p. 609). He believes that the resistance is due to the destruction or the attenuation of the virus by contact with living nerve cells, although the formation of antibodies, and the action of leucocytic enzymes appear to play a part.

iv. *Methods of treatment and statistics.*

A sixth review of statistics furnished to the League of Nations by the different institutes is submitted by MCKENDRICK.[22] The main fact which emerges is the remarkable degree of homogeneity indicated in the following Table, which includes statistics compiled from the series of six reviews.

From an examination of this Table it appears that the numbers in the non-European group (for which the percentage mortality is 0·72) are in general insufficient to detect superiority of one treatment as compared with another when the excess relative efficiency of the better treatment is about 10 or 15 per cent. : whilst in the case of Europeans (for which the average mortality is 0·16) the corresponding figure is about 25 per cent. It is thus reasonable to conclude that it is unlikely that a difference of efficiency of more than 25 per cent. between any two methods of treatment exists. Thus the conclusion is arrived at that the figures so far available are not yet sufficient to detect the existence of differences of less than 25 per cent. It may at first sight seem surprising that figures amounting in all to about half a million

[20] BUSSON (B.). Das Uebertreten und die Speicherung von Virus fixe im Zentralnervensystem geimpfter Menschen und Tiere.—*Zent. f. Bakt.* I. Abt. Orig. 1935. Dec. 9. Vol. 135. No. 6. pp. 331–341.

[21] JONNESCO (Démètre). Contribution à l'étude de l'immunité naturelle du chien contre la rage.—*C. R. Soc. Biol.* 1936. Vol. 121. No. 12. pp. 1203–1205.

[22] MCKENDRICK (A. G.). A Sixth Analytical Review of Reports from Pasteur Institutes on the Results of Anti-Rabies Treatment.—*Quarterly Bull. Health Organisation. League of Nations.* Geneva. 1935. Dec. Vol. 4. No. 4. pp. 752–786.

	Number treated	Deaths		Mortality per cent.
		Observed	Calculated*	
Europeans				
1. Cords	40,522	66	66	0·16
2. Dilutions ...	43,218	85	71	0·20
3. Killed phenol ...	34,034	51	56	0·15
4. Live phenol ...	2,268	5	4	0·22
5. Fermi's vacc. ...	5,123	12	8	0·23
6. Fermi's sero-vaccine	255	0	0·4	0
7. Heated vaccine ...	67,664	120	111	0·18
8. Killed ether ...	46,547	65	76	0·14
9. Mixed	41,358	51	68	0·12
10. Yatren	5,384	13	9	0·24
	286,373	468	469	0·16
Non-Europeans.				
1. Cords	33,915	225	244	0·66
3. Killed phenol ...	185,766	1,353	1,334	0·73
	219,681	1,578	1,578	0·72

* Calculated from the average mortality.

are insufficient to demonstrate differences of this order in the efficiencies of various methods of treatment. "The controlling factor is the mortality rate; the lower this may be, the greater the number of patients required to demonstrate variations. In the case of rabies [statistics], as shown above, the mortality rate [amongst the treated] may be as low as 0·16 per cent." It appears also that the liability to paralytic accident is 1 in 10,372 in the case of those treated by killed vaccines, as compared with 1 in 2,632, amongst those treated by live vaccines, and 1 in 11,637 amongst those treated by heated vaccines (Babes).

The statistics for the Institute Camara Pestana (Lisbon) for the years 1921–34 are considered by PEREIRA DA SILVA.[23] During this period four different methods were employed and the combined results were as follows. The statistics refer only to persons belonging to categories A, B and C.

Years	Method	Number treated	Deaths	Percentage mortality
1921–24	Dried cords (Pasteur)	7,528	25	0·33
1924–25	Dilutions (Hogyes)	4,207	16	0·38
1925–27	Ether vaccine (Alivisatos-Pereira da Silva) ...	1,164	2	0·17
1925–34	Killed phenol vaccine (Semple-Pereira da Silva)	8,461	4	0·047

[23] PEREIRA DA SILVA (E.). Le traitement antirabique à l'Institut Câmara Pestana (1921–1934).—*Arquivos Inst. Bact. Camara Pestana.* 1936. Vol. 7. No. 2. pp. 225–234. With 2 graphs.

[It is to be noted that the numbers treated annually have fallen from a maximum of 3272 in 1925 to 254 in 1934, and that the numbers of dogs' brains examined and proved to contain the virus has similarly declined from 230 in 1925 to 3 in 1934. It would consequently be unwise to assume that the reduction in mortality was due solely to the alterations in the method of treatment. The author expresses no opinion.]

Vazquez-Colet[24] reports upon antirabic treatment at Manila during the period 1914–33. From 1914 to 1927 the vaccine consisted of 3-day cords emulsified in 0·5 per cent. phenolized saline. During the remaining years a 1 per cent. emulsion of fresh brain and cord in carbolized salt solution was employed. In each case treatment was given for 25 days.

During the period 1914–27 when 3-day cords were employed "there were treated 6,266 cases bitten by dogs, of which 5,716 were Filipinos, and 8 of them (Filipinos) developed hydrophobia. Only 3,450 of the Filipinos bitten by dogs took complete treatment, and of the 8 that developed hydrophobia only 3 took complete treatment, giving a death rate of 0·08 per cent. From 1928–33 carbolized vaccine was used. During this period there were treated 11,343 cases bitten by dogs, of which 10,743 were Filipinos and 6 of them (Filipinos) developed rabies. Only 4,700 of the Filipinos bitten by dogs took complete treatment, and of the 6 cases that developed only 2 received complete treatment giving a death rate of 0·04 per cent. The figures show that with the use of the dried cord the incidence of hydrophobia was twice as great as with the use of carbolized vaccine."

The author in his summary states that "a comparison of the efficiency of the two types of vaccine employed brings out the fact that with the use of the 3-day cord the incidence of hydrophobia among the cases was twice as great as with the use of the carbolized vaccine." [As a matter of fact a difference in mortalities as great or greater than that observed would be likely to occur about once in two times on the assumption that the two vaccines were in fact equally efficacious. It is amazing that in the present state of knowledge the author should have laid any weight upon this observation.]

In Palestine[25] the treatment of rabies has been completely decentralized. There are now 31 provincial centres. During 1934, 1,039 bitten persons have received a full course of antirabic treatment by Semple's method, and amongst these 5 cases of rabies have occurred. The mortality rate is 0·48 per cent., as compared with 0·13 in the previous year. No neuroparalytic accidents have been observed.

v. *Rabies in Animals.*

The question of the control of rabies in wild animals with special reference to the conditions prevailing in South Africa was discussed at the Pan-African Health Conference at Johannesburg.[26] It was

[24] Vazquez-Colet (Ana). The Pasteur Antirabic Treatment at the Bureau of Science, Manila.—*Philippine Jl. Sci.* 1935. Aug. Vol. 57. No. 4. pp. 435–442.

[25] Palestine, Department of Health. Annual Report for the Year 1934. [Rabies pp. 40, 92–95.]

[26] Quarterly Bulletin of the Health Organisation. League of Nations. Geneva. 1936. Mar. Vol. 5. No. 1. pp. 161–165.—Animal Diseases communicable to Man. A. Rabies. [Report of Committee on Diseases conveyed by Animals to Man and Resolutions of Pan-African Health Conference, Johannesburg, Nov. 20–30, 1935. pp. 161–162.] Du Toit, (P. J.). Wild Carnivora as Carriers of Rabies. [Annex pp. 162–165.]

recommended " that further research be undertaken in connection with the transmission and eradication of rabies, and that the biology of the small carnivora should be studied with a view to the elaboration of some method of destroying them." In an annex the rôle played in the spread of rabies in South Africa by animals belonging to the family *Viverridae* (meerkat) is discussed by Du Toit.

It is proposed to study the practical aspects of prophylactic vaccination of dogs in Indochina.[27] An installation has been set up for this purpose. The formolated vaccine of Plantureux will be used.

In a general paper Schoening[28] discusses the place of prophylactic immunization of dogs in the control of canine rabies. If treatment were cent. per cent. effective, and if every dog were treated, then prophylactic immunization of dogs would be successful as a sole means of controlling rabies. As this is not the case, prophylaxis must be supplemented by licensing, quarantine and the impounding and disposal of stray dogs.

vi. *Miscellaneous.*

Levaditi and Schoen[29] find that street virus has an " elective affinity " for the neoplastic cells of Pearce's carcinoma. Tumours were grafted in the anterior chamber of the eye and in the testicle, and street virus was inoculated into the brain or under the cornea of the opposite side. Absolutely typical Negri bodies appeared in the neoplastic cells. Thus in the opinion of the authors Negrigenesis is not confined solely to neurones and corneal epithelium, but occurs also in epithelial new formations.

Greval[30] draws attention to the fact that in certain instances biting animals may have an unusually high degree of infectivity, and quotes a case in which 3 out of 4 persons bitten by the same dog succumbed to rabies. One received treatment, but it was not commenced until 55 days after the bite.

He then describes an untreated case which terminated fatally. The patient was owner of the dog in question, and was in the habit of playing with it. " He admitted that he had often been licked whilst playing with the dog, and said that the only possible way he might have got any dog's saliva in contact with abrasions on his skin was possibly when he rubbed his cheeks and hands after shaving." There were no visible cuts or abrasions when he was examined, and he was not sent for treatment. The case was an unfortunate one, but the evidence is hardly strong enough to lead one to the conclusion that infection through the unbroken skin is possible. Greval then discusses 4 cases of sequelae after treatment by Semple's vaccine of which two showed paralytic symptoms ; the first involved the bladder and rectum, and the second was of the usual bulbar type. The symptoms in both cases were temporary, and recovery was complete.

---

[27] Recueil de Médecine Vétérinaire Exotique. 1935. July–Sept. Vol. 8. No. 3. pp. 118–123.—Organisation d'un service d'étude de la vaccination antirabique des chiens en Indochine.

[28] Schoening (H. W.). Can the Health Officer Safely Utilise Prophylactic Immunization as the Sole Means to control Canine Rabies ?—*Amer. Jl. Public Health.* 1936. Mar. Vol. 26. No. 3. pp. 265–267.

[29] Levaditi (Constantin) & Schoen (Rachel). Virus rabique et cellules néoplasiques.—*C. R. Acad. Sci.* 1936. Feb. 24. Vol. 202. No. 8. pp. 702–704. With 3 figs.

[30] Greval (S. D. S.). Against Orthodoxies in Rabies.—*Indian Med. Gaz.* 1936. Feb. Vol. 71. No. 2. pp. 69–74. [15 refs.]

The pathogenity of the Chinese Hamster to fixed virus rabies is the subject of a communication by YEN.[31] The incubation period varied between 5 and 8 days, and the symptomatic picture was similar to that observed in the rabbit. Negri bodies measuring 4 to 6 μ were found in the usual situations. The virus has been carried to the 10th passage in this animal.

An outbreak of rabies is reported by GODDING[32] from British Somaliland. Four persons in the Bovama district have died of the disease, and various species of animals including an Aardwolf (*Proteles cristabus*) have been involved. It is stated that rabies is endemic in Abyssinia, and that the incidence of the disease in Harar and Jigjiga is at the moment above normal. Every precaution has been taken to prevent further spread of the disease, but "Abyssinia remains a potent source of infection." This is the first time that rabies has been reported from the Somaliland Protectorate. *A. G. McKendrick.*

---

[31] YEN (Albert C. H.). Experimental Virus Infections in Chinese Hamster. I. Susceptibility to Fixed Rabies Virus.—*Proc. Soc. Experim. Biol. & Med.* 1936. Apr. Vol. 34. No. 3. pp. 315–318.

[32] SOMALILAND PROTECTORATE : ANNUAL MEDICAL & SANITARY REPORT FOR THE YEAR ENDING 31ST DECEMBER, 1934. Appendix II. pp. 93–98.—Report on an Outbreak of Rabies at Borama, June–October, 1934 [GODDING (H. C.)].

MALARIA.

SINTON (J. A.). **What Malaria costs India, Nationally, Socially and Economically.**—*Records of the Malaria Survey of India.* 1935. Sept. & Dec. Vol. 5. Nos. 3 & 4. pp. 223–264; 413–489. 1936. Mar. Vol. 6. No. 1. pp. 91–169. With 1 chart. [10 pages of refs.]

Colonel Sinton has collected in this series of papers a great deal which has been written about the evil effects of malaria in India and in other parts of the world. He has attempted to assess in terms of money the value of the work the malaria-stricken people leave undone, the loss on the work they do badly, the cost of the medicine they drink, the cost of their funeral expenses and so on, and has added the results together to make an enormous total. Alcohol, rats and other evils have been treated statistically in a similar manner, but we are indebted to Colonel Sinton for telling us what is often forgotten in many a malaria-survey which records the spleen measurements to several places of decimals—that is, the effect of the disease upon the health and happiness of the people.

Colonel Sinton makes out his bill of charges under four heads: (1) The effect of malaria upon the natural increase of the population. (2) Its effect upon the health and vitality of the people. (3) Its effect upon the social, intellectual and political progress of the nation. (4) Its effect upon the economic, agricultural and industrial development of the country. He then attempts to estimate the financial loss which the disease causes to India and whether it would pay to undertake measures to control it. He finds that malaria lowers the birth-rate by reducing the number of conceptions and by causing abortions and still-births. He quotes evidence that impotence is common in water-logged villages and in the malarious parts of the Terai. In a record of the year 1870, concerning villages along the Western Jumna Canal, it was stated "The unfruitfulness of women is a subject of common remark, and the consequent difficulty of inducing other Jat families to give their daughters to the men of Panipat and the environs of the canals generally is very great." As regards abortions, it has been estimated that, in Bengal alone, the potential population is lessened annually by 800,000 persons from this cause, and that 37·8 per cent. of these abortions are due to malaria.

Malaria raises the death rate not only directly, but also indirectly; by lowering the general vitality of a community it prepares the ground for other diseases, and is responsible for many a death of which it is not actually the immediate cause. The author considers that "it seems probable that malaria, by its direct and indirect actions, is responsible for at least 2,000,000 deaths each year in India."

One must admit that Colonel Sinton has demonstrated that the population of India would be very much larger than it is, if it were not for the annual sacrifice which is paid to malaria; but will this argument stir the administrator to enthusiastic action? On page 465, one reads, "During the 60 years which have elapsed since the first Indian census was taken in 1872, the population of this country has increased by 46·6 per cent. . . . As a result, a problem of the greatest national importance has arisen, as to how these increasing millions are to gain a decent livelihood in the future." The author's answer to this question

is that the disease cannot be considered as a healthy pruning ; it attacks both fit and unfit indiscriminately, and those it does not kill, it often leaves maimed and crippled to swell the ranks of the unfit.

In connexion with the evil influence of malaria on the physical development of children and adults we find a very pleasing quotation, evidently from America : " Every once in a while somebody rises up to criticise modern parents for devoting too much time to their children's physical being (as compared with their spiritual and educational). . . . Our righteous ancestors disregarded their bodies and paid attention to their souls, and it might be added that by neglecting their bodies in the interests of their souls, they beat us to heaven by an average of twenty years."

The author computes the number of persons suffering annually from malaria, in India, at the high figure of one hundred million ; in addition to this there are those suffering from " an indirect morbidity predisposed to by this disease which may be between 25 and 75 million cases. . . . Apart from the economic loss caused by the action of malaria upon the mental state of the population, this disease has the deplorable effect of hindering greatly the intellectual, social and national development of many people afflicted by it." The cost of medical attendance in respect of malaria in India is assessed at £15 million per annum, the loss in wages at £18 million, the loss from ' post-malarial inefficiency ' at £22 to £55 million, ' unprofitable funeral expenses ' £500,000, economic loss from deaths directly due to malaria £67½ million sterling. Beyond all this there are the financial losses of the community in respect of the value of houses and land, and a hundred other things, to be taken into consideration. Agriculture loses incalculable sums because of the action of malaria in causing loss of work, and the abandonment, imperfect cultivation, or retarded development of large fertile tracts. Why is malaria productive of so much suffering in rural India when it causes comparatively little illness in Africa among natives living in hyperendemic areas, as Garnham of Kenya and Wilson of Tanganyika have told us ? The loss caused by malaria to the development of mining industries, and the effects of malaria on the railways are next taken into consideration. So the bill grows, and one cannot help wondering what would happen if it could be liquidated—if malaria could be conjured away. Would India be transformed into a Garden of Eden, or would there be a hitch somewhere, the kind of horrid snag which comes into stories like " The Monkey's Paw " ?

William Fletcher.

SINTON (J. A.). **Malarial Prevalence in its Relationship to the Problems of Food Supply and Increasing Population in India.**—*Records of the Malaria Survey of India.* 1936. Mar. Vol. 6. No. 1. pp. 53–65. [34 refs.]

The increase of population has outstripped food production. Fertile tracts remain uncultivated because of malaria. Poor living and malaria have made the peasants so dull and lethargic that they are without initiative. " It would pay India to commence a more intensive anti-malaria campaign."

The population of India is now about 353,000,000. It has nearly doubled within the last 60 years. It has been said by the Government Agricultural Chemist, Mr. Viswa Nath, that India's food production is

sufficient for only two-thirds of her population. This means an exceptionally low standard of living. The solution of this problem depends largely upon (1) An increased production of food stuffs ; (2) An increase in industrialism and the development of the natural resources of the country.

Compared with agriculture, the other industries of India are of minor importance, no single factor is so important as the increase of the locally grown food supply. Much of the most fertile land is also the most malarious, and malaria is the chief disease which hinders the expansion of agriculture. Italy in reclaiming the Campagna has recently given an example of the way in which this problem can be solved. In India, many large fertile tracts have remained uncultivated because of malaria. Care must be taken that no hasty attempts to colonize are undertaken before the areas have been rendered fit for occupation by means of antimalaria work. In the scheme for the colonization of Palestine after the war, swampy, fertile tracts were acquired by the promoters, and they were occupied without preparation. The results were disastrous, but, by the introduction of proper malaria-control measures, disaster was eventually transformed into success. The colonizing agencies now realize that it is a bad practice to settle people in malarious areas until provision has been made to render these areas habitable. There seems little hope of any satisfactory advance in the extension and improvement of agriculture in India " so long as the rural populations continue to bear this enormous burden of malarial sickness, that is sapping both their physical and mental activities." *W. F.*

NIEUWENHUIS (A. W.). Körperliche und kulturelle Volksentartung in Gebieten endemischer Malaria. Mittel-Sumatra. [**Physical and Cultural Race Degeneration in Endemic Malarial Regions, Central Sumatra.**]—*Janus.* 1934. Vol. 38. pp. 121–136 ; 163–178 ; 193–211 and 1935. Vol. 39. pp. 37–48 ; 94–104 ; 127–134 ; 212–218. With 1 folding map.

The author considers that central Sumatra offers very good facilities for studying the problems stated in the title. Because endemic malaria is the most important of the deleterious influences there, and it is rampant in the eastern plains, but the western Barisan high mountains are free from endemic malaria. As a result the Malayan population of the eastern half is very small, whereas the mountains of the west are very populous ; also in culture the same difference is noted, high in the west, low in the east.

He quotes the observations of Doorenbos on the vectors of malaria in Sumatra. 243,137 mosquitos were caught and classified on the east coast of Sumatra ; the result of 80,667 dissections is described. The highest infection rates for the different species of anopheles are :—

					Per cent.
M. sinensis ...	Londut, December 1930	...	5 out of	41	12·2
C. kochi	Ajer Poetih, 1 October 1926	...	9 ,,	59	15·3
M. aconita ...	Colt Estate, April 1928	...	3 ,,	26	11·5
N. leucosphyra	K. Piasa, October 1925	....	4 ,,	101	4·0
N. maculatus	Londut, November 1928	...	9 ,,	53	17·0

He deals also with the anthropological studies in Sumatra by Drs. Kleiweg de Zwaan and Alfred Maas.

This monograph is a mine of information and deals with most important scientific and practical problems. It should be consulted in the original by those interested. *E. D. W. Greig.*

Rivista di Malariologia. Sez. I. 1935. Vol. 14. No. 6. Supplement. 114 pp.—Conferenze sulla malaria tenute nell'agosto del 1935. [**Conference on Malaria, Rome, August 1935.**]

Malaria therapy and research. Immunity due to latent infection. Importance of repeated inoculation in the production of immunity. Prophylaxis by drugs. Dangers of plasmoquine. Disappearance of malaria due to change in race of anopheles. Housing and malaria. Testing drugs on bird malarias. Kikuth's belief in direct action of quinine. Integral bonification and "*bonifica umana preepidemica.*"

The first paper in this series is written by M. Ciuca; it concerns the service which therapeutic malaria has rendered to the proper understanding of the disease. Investigations are being carried out in Rumania at the malaria-therapy station, established with the help of the Rockefeller Foundation, in connexion with the mental hospital at Socola.

The second paper deals with immunity in malaria, and is by the same author. As illustrations of the development of immunity in a population he instances the immunity of adult Indians in certain parts of the United Provinces and elsewhere, which has been acquired at the cost of the sacrifice of an enormous number of children in infancy. [Communal immunity in Africa is attained without so great a sacrifice, see Wilson, below p. 765]. The author has found that a latent infection is present in 60 per cent. of benign tertian immunes and in 100 per cent. of subtertian and quartan immunes. These figures were obtained as the result of tests made by inoculating patients' blood into non-immunes; but it does not always follow that an individual is entirely free from parasites because no infection results from the inoculation of his blood. A latent infection following a first injection does not necessarily confer immunity. The important factor in immunity is repeated inoculation.

The third paper, which concerns the relative value of different drugs, is also by M. Ciuca. As a result of his studies at Socola, he agrees with the malaria commission of the League of Nations that the method of choice in clinical prophylaxis is the administration of a daily dose of 5 grains of quinine during residence in a malarious district and for several months after leaving it. A daily dose of 0·1 gram of atebrin could be employed in the same way, but it has the disadvantage of staining the skin yellow. The author treated a number of patients, some suffering from naturally contracted and some from therapeutic malaria, with the following doses: (*a*) Atebrin 0·3 gram, (*b*) Quinine 1 gram, (*c*) Atebrin 0·3+quinine 0·5 gram, (*d*) Atebrin 0·3+plasmoquine 0·02 gram. The duration of the treatment was 7 days in each case. In the treatment of benign tertian and quartan, quinine and atebrin were equally efficacious, but there were fewer relapses after atebrin. In the treatment of subtertian, atebrin appeared to be somewhat better than quinine, and it should be employed in all severe attacks which are resistant to that alkaloid. Atebrin and quinine given together did not act better than either drug given alone. In quartan malaria there were fewer relapses after atebrin+plasmoquine than after other drugs, but this was not the case in benign tertian (but

see SINTON, *ante*, p. 688). In any case, according to the author, the mixture atebrin+plasmoquine is so apt to be toxic that it should never be employed.

The fourth and fifth papers are by L. W. HACKETT concerning the Races of *Anopheles maculipennis*, the Natural Disappearance of Malaria and the Methods of Attacking Malaria. Discussing biological methods of control he writes that animal barriers can be of use only when those anopheles are concerned which feed by instinct on animals ; such, for example are *messeae*, *melanoon*, *typicus* and *atroparvus* ; *elutus* and *labranchiae* are never deviated by cattle. On the east coast of England where cases of malaria occurred during the war, JAMES noticed that anopheles stayed in houses and continued to feed during the winter. This he ascribed to the darkness and poor ventilation of the houses which encouraged the mosquitoes to remain there. Now it is known that this phenomenon was due, not to the faulty character of the houses, but to the presence of the *atroparvus* race of *A. maculipennis* which does not go into hibernation, but shelters in dwellings and continues to feed through the winter. In central England, another race is present which winters in uninhabited buildings, ceases to feed and goes into complete hibernation. Disappearance of malaria is sometimes due to a change in the anopheline fauna. For example, in the Po delta *elutus* was formerly present, but irrigation and agriculture have modified conditions in favour of *atroparvus*, which is not a carrier in this district, and *atroparvus* has ousted *elutus*, to the great benefit of the district. In the polders of the Low Countries, *atroparvus* breeds in the brackish lagoons, but when the lagoons are cut off from the sea and fresh water is continually running into them, they gradually become fresh water lakes and *atroparvus* is supplanted by *messeae*. At Durazzo, the port of Albania, there was a large brackish lagoon which could not be treated in this way because no large rivers ran into it. The author dealt with this by fixing automatic sluice-gates which admitted the sea water but did not let it out again, and, in the course of two years, the salt content of the lake had increased, through evaporation, to such an extent that *elutus* could breed in it no longer. Again, the author has observed, during the last two years, the gradual replacement of *elutus* and *labranchiae* by *messeae* and *melanoon* in the Pontine Marshes. *Maculipennis* does not appear to be the only anopheline which consists of several races. There are others, for example, *ludlowi*, *hyrcanus*, *maculatus* and *pseudopunctipennis* which behave as dangerous carriers in some countries, but are quite harmless in others, and it may be that these species, too, contain different races.

W. KIKUTH contributed a paper on Experimental Immunology and the testing of drugs on the malarias of birds and monkeys. He found that plasmoquine, administered to Java sparrows infected with *Haemoproteus*, caused the disappearance of gametocytes from the blood. They soon returned, because the plasmoquine had no effect on the schizonts in the tissues, but, when the schizonticide, atebrin, was given in addition, the schizonts were destroyed and there were no more relapses. The author does not believe that either quinine or the synthetic drugs act indirectly ; he states that more and more evidence is being accumulated in favour of the direct action of these drugs on the parasites.

Dr. LUTRARIO described the Hygiene Organisation of the League of Nations which includes the Malaria Commission, of which he is President, the Cancer Commission and other bodies.

Professor Ottolenghi dealt with the question of prophylaxis by means of drugs, and gave instances of excellent results which had been obtained by giving courses of mass treatment at the end of the spring, before the beginning of the malaria season. Very good results were obtained at Ferrare with a ten-day course of plasmoquine and quinine. (First 2 days, plasmoquine 0·03+quinine sulphate 0·9. Third day, plasmoquine 0·02+quinine 0·6. Fourth to tenth day, plasmoquine 0·01+quinine 0·3 gram.) Atebrin+plasmoquine has also been used with success in this *bonifica umana preepidemica.*

Professor Ottolenghi also discussed the question of *grande bonification* and emphasized the importance of regulating the supply and flow of water. The disappearance of *elutus* from the region of Ferrare he ascribes to a change in the chemical composition of the water which has been rendered less saline owing to abundant irrigation with river water. Malaria control is only a part of bonification. When the work of reclamation is first begun, it is necessary to push on with the main drainage schemes as quickly as possible and during this period it is necessary to prosecute vigorous antimalaria operations, but as the land is developed and settled with men and beasts, less and less antimalaria work is necessary. *W. F.*

Pecori (G.) & Escalar (G.). Relazione della campagna antimalarica nell'Agro Romano durante l'anno 1934. [**Report of the Antimalaria Campaign in Agro Romano during 1934.**]—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 6. pp. 469–519. With 2 graphs & 1 map.

The main points only of this detailed report can be referred to here. By the beginning of the year there were 34 sanitary stations each with its medical officer and staff and the whole under the central Directorate of the Government Bureau of Hygiene. In the Agro were 101 schools with 8,000 pupils. As in preceding years the campaign included quininization, mechanical protection, destruction of larvae and adult mosquitoes, and zooprophylaxis, and these were applied according to the gravity of the endemicity, the prevalence of anopheles and so forth. Antilarval measures were carried out in 20 zones, quinine prophylaxis in 15, and the malaria attack rate was only 0·7 per cent. Blood examinations totalled 70,000. Incidence, including primary cases and relapses, was 1·99 per cent. (1·98 in 1933) ; primary cases were 0·9 per cent. of the population (0·6 in 1933) ; this increase applied to benign tertian infections only, malignant tertian definitely was less, so that the author states " the incidence of infection continued, as in the two preceding years, to fall." Zooprophylaxis, at Ardea, has resulted in a further diminution of malaria among the inhabitants of this village, from 7·5 per cent. in 1933 to 5·3 ; prior to the institution of this measure the incidence was 32·2 per cent. *H. H. S.*

Sergent (Edm.), Sergent (Et.), Parrot (L.) & Catanei (A.). Etude épidémiologique du paludisme. Technique des indices endémiques. [**The Technique of Endemic Indices.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. Dec. Vol. 13. No. 4. pp. 566–576. With 7 figs. (1 map) & 3 plates.

This is an instructional pamphlet.

It is necessary, before undertaking a malaria campaign, to estimate the amount of malaria present in the locality. This is done by determining the following indexes: (1) *The Splenic Index*: this is the percentage of children under 15 with enlarged spleens palpable below the costal margin. (2) *The Splenometric Index*: the projection of each spleen below the costal margin is measured in finger breadths. Spleens up to one finger-breadth are measured as 1, spleens up to 2 finger-breadths as 2, and so on; all spleens above 5 finger-breadths are measured as 6. The average size of the enlarged spleens is given by adding together all the finger-breadths and dividing by the number of enlarged spleens examined. The splenometric index is obtained by multiplying this figure by the splenic index. That is to say, the splenometric index = the percentage of enlarged spleens × the average size of the enlarged spleens measured in finger-breadths. For example: if there were 40 per cent. of enlarged spleens and the average size were 2 finger-breadths, then, the splenometric index would be 40×2. It indicates not only the prevalence of enlarged spleens, but also the degree of enlargement. It is particularly useful in assessing the value of anti-malaria measures in places where the splenic index is high and the spleens are very large. Here, the splenic index alone would not detect an improvement indicated only by a general decrease in size of the enlarged spleens, if they remained palpable. (3) *The Parasite Index*: is the percentage of children under 15 in whose blood parasites are found during a single examination of a thick drop preparation for a fixed period of 5 to 10 minutes. (4) *The Endemic Index of Ross*: This is obtained as follows: the number of children with parasites in their blood + the number of children with enlarged spleens but no parasites, is divided by the total number of children examined. This index is a useful complement to the splenic and parasite indexes and is particularly useful in the comparison of different localities. (5) *The Sporozoite Index*: this is the percentage of anopheles with sporozoites in their salivary glands. The following technique is recommended: remove the legs and wings of the mosquito; fix the thorax by transfixion with a pin; seize the head with fine forceps and pull it off; two shining drops are visible at the back of the head, these are the salivary glands; spread them out on a slide. Sometimes the glands remain in the thorax; in this case squeeze the thorax, and make a film with the fluid which exudes at the place where the head was cut off. It is advisable to do this in any case, even when the glands come away with the head.

W. F.

Quintana Otero (Fernando). El problema del paludismo en la cuenca del Esla (Zamora). [**The Malaria Problem in the Esla Valley (Zamora).**—*Medicina Países Cálidos.* Madrid. 1936. Apr. Vol. 9. No. 4. pp. 160–187. With 5 figs. & 1 map.

As a result of investigations carried out in the Zamora Province the author concludes that among the riparian settlements of the Esla dam conditions for malaria are present, larvae of *A. maculipennis* have been seen in the pools and deposits about the houses, and adult forms in the stables and pigsties near human dwellings in some of the settlements; cases of indigenous malaria are met with, that among the people are infected persons coming from other parts when the malaria endemicity is great; that this conjunction of circumstances aggravates the local liability to infection.

In the Aliste valley, however, malaria is not endemic, and the splenic index is nil. There are excellent breeding sites for mosquitoes in Vegalatrabe, Vide and Losacino—small collections of water, clear, undisturbed and covered abundantly with vegetation—but they hardly persist during the spring and in the summer disappear altogether; if there are heavy rains they collect again in September. Hence usually one, perhaps two generations only of mosquitoes are produced in the spring, and again in the autumn. This interruption of the biological cycle during summer is held to account for the absence of endemicity. The following are, in sum, the author's conclusions :—

1. Anophelism at the present time among those living in the Esla valley is small and limited to part of the warm season.
2. In the pasture lands the mosquitoes breed abundantly and continue to do so in the summer.
3. Among the inhabitants malaria is practically entirely sporadic.
4. The dam is a source of danger only in so far as it increases the number of breeding sites or prevents those already existing from drying up.
5. The remedies are (1) to drain the borders so that collections are not left when the dam is emptied, (2) to treat cases. *H. H. S.*

Carr (Henry P.), Mandekos (A.) & Barber (M. A.). **Malaria Studies in Greece. A Survey of Malaria Morbidity in a Region of East Macedonia.**—*Ann. Trop. Med. & Parasit.* 1935. Dec. 18. Vol. 29. No. 4. pp. 399–405.

There is a high degree of tolerance of infection in this district; though many were infected, few were incapacitated.

The purpose of this survey was to obtain information as to the amount of actual illness due to malaria in East Macedonia. Nineteen villages representing various degrees of malarial endemicity were visited during the malaria season, between August and October. The presence of parasites or an enlarged spleen did not necessarily indicate illness: in some of the villages, 60 per cent. of the children who were quite fit to attend school had parasites in their blood, and 80 per cent. had enlarged spleens. "With regard to the amount of recognizable clinical malaria in the whole survey, the totals . . . indicate less than 2 per cent. clinically ill, including parasite positives and negatives. Among parasite positives the percentage is under 1." These percentages represent the findings at one visit. Repeated visits would doubtless have detected a much larger number of sick. In a group of villages with a population of 2,089 where malaria was highly endemic, only 3·5 per cent. were found wholly or partly incapacitated, at the time the survey was made, and not all of these cases were suffering from malaria. There was less illness in villages where endemicity was low than in those where it was high. *W. F.*

Timbres (Harry G.). **Studies on Malaria in Villages in Western Bengal.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 345–370. With 5 graphs & 1 map.

A. philippinensis is the chief vector. Benign tertian and quartan infections are common.

This malaria survey was made in 7 villages situated in the District of Birbhum, Bengal. It was continued for 89 weeks, from July 1932 to April 1934. It was made possible through the help of the Institute of

Rural Reconstruction, which is the Village Work Department of the Visva-Bharati founded by Dr. Rabindranath TAGORE and the American Friends Service Committee of Philadelphia who lent the services of the author. The population of the villages numbered 2,582. It is on the whole a hyperendemic area. The distribution of types of malaria in the autumn and spring epidemics was as follows: August to December, *vivax* 58·2 per cent., *falciparum* 33·2, *malariae* 8·6; January to May, *vivax* 47 per cent., *malariae* 31·2, *falciparum* 21·8.

A. culicifacies, *A. minimus* and *A. aconitus*, carriers in other parts of India, were relatively scarce and never found infected. The chief carrier in the summer and autumn was *A. philippinensis*; the only other carriers of importance were *A. annularis* and *A. pallidus*. *A. pallidus* was the only species found infected during the cold-weather months preceding the spring epidemic. *A. annularis* was very numerous at this time; *A. philippinensis* was very scarce. All three species bred in still, clean, shady water with aquatic vegetation. Rice fields were not important breeding places.

An experiment with plasmoquine and quinine was carried on for six months in the four central villages of the group. "The object was to see if partial 'plasmoquinization' of those persons most likely to harbour gametocytes would have any noticeable effect in reducing the incidence of malaria." During the time the drugs were being given there was less malaria, and the sporozoite rate was lower in this group of villages than in the three peripheral villages forming the control group, but the author is of opinion that the results of the experiment were inconclusive. *W. F.*

SINTON (J. A.). **"Man-Made" Malaria in India.**—*Indian Med. Gaz.* 1936. Apr. Vol. 71. No. 4. pp. 181–187. [37 refs.]

Emphasizes the harm done by large irrigation schemes planned without due regard to drainage.

The effects of human activities in increasing the prevalence of malaria are considered under the following heads:—

A. Conditions leading to economic stress and lowered resistance. Example: severe economic stress which follows the water-logging sometimes caused by large engineering works.

B. Introduction of human carriers into a healthy area, or of susceptibles into a malarious area. Example: aggregations of tropical labour in connexion with large industrial, engineering, mining, or other projects. The infection is liable to spread from the labourers to the surrounding inhabitants. *C. Measures resulting in an increase of anopheles.* (*a*) Local Activities. Examples: Ornamental tanks and fountains in Delhi. Cisterns and wells in many towns. Borrow-pits, bad drainage, badly controlled water supply, dripping taps. (*b*) Wide-spread activities causing increase of water. Examples: Local excavations in connexion with engineering works. Obstruction to natural drainage by the construction of roads and railways. Introduction of large irrigation projects without the provision of proper drainage. Improper use of irrigation water. Leaking irrigation channels. The water-logging Board of the Punjab have issued a statement of the "principles to be observed in the preparation of canal projects," but, unfortunately, these principles appear to have been ignored, and enormous losses have resulted—decreased prosperity of the population, decreased fertility of the land and decreased health

of the people have been caused by the neglect of proper precautions. (c) Widespread activities causing decrease of water. The great example of this is in lower Bengal where large areas which, in the past, were covered by silt-bearing water from the Ganges at certain seasons of the year, have now been deprived of this irrigation. This inundation-irrigation was stopped by the building of embankments, roads and railways, with the result that anopheles breed in the pools and dead ends of the old drainage-canals, and, for lack of river-silt, the land is impoverished. The people are sunk in poverty and a vast proportion of them suffers each year from recurring attacks of malaria. The author discusses the remedies for these malaria-producing conditions, and emphasizes the importance of co-operation between different government departments. *W. F.*

Morin (Henry G. S.). A propos de certains échecs de la prophylaxie antilarvaire du paludisme. [**Certain Failures of Antilarva Methods of Prevention in Malaria.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1936. Mar. Vol. 14. No. 3. pp. 327–329. With 4 figs.

An illustrated warning that failure to achieve adequate results by drainage, as an antimalaria measure, is sometimes attributable to faulty construction and even more to negligence in upkeep.

Norman White.

Health Briefs. 1935. Nov. 15. Vol. 12. No. 11. pp. 3–4.—Malaria Control.

Ejercito (Antonio). Present Orientation in the Control of Malaria in Tropical Countries.—*Jl. Philippine Islands Med. Assoc.* 1936. Feb. Vol. 16. No. 2. pp. 61–71. With 5 figs. on 2 plates.

Schwietert. Ueber einen neuen Fall von endemischer Malaria tertiana. [**Another Case of Endemic Malaria (in Germany).**]—*Deut. Med. Woch.* 1936. May 29. Vol. 62. No. 22. p. 898.

From March to August 1935 the patient was working in Emden, but enjoyed good health all the time. He then moved to Weilburg an der Lahn and a month later fell sick with a shivering attack, the next day there was no fever, but repeatedly thereafter, every other day, he had fever, and the blood picture and the symptoms were those of the classical tertian malaria. The symptoms cleared up when quinine was given but relapse occurred soon after he left hospital. The author discusses the question of place of infection and concludes that it must have been Emden, which is one of the few remaining endemic foci in Germany to-day. *H. H. S.*

Despujols (B. P.). Le paludisme autochtone dans la 18e région. [**Indigenous Malaria in Bordeaux.**]—*Rev. Service Santé Milit.* formerly *Arch. Méd. et Pharm. Milit.* 1936. Mar. Vol. 104. No. 3. pp. 419–445. With 3 figs. [12 refs.]

The city of Bordeaux is situated amid great marshes on the banks of the Garronne; during the Middle Ages, there were repeated epidemics whenever any work was undertaken to drain these marshes and enlarge the town. In 1895, there was an outbreak when the docks were being

extended. In 1921, six cases were observed in children who had never left the town ; 6 cases occurred at the same time among soldiers, 3 of whom were living in the camp of Songe, 20 kilometres from Bordeaux. In 1934, there was a small epidemic in this same camp during the second half of August. It has been suggested that an indigenous strain is responsible, but the author thinks that the small outbreaks are probably due to infections introduced by African troops and by soldiers returning from the colonies. *W. F.*

Sieburgh (G.). De malaria te Oosthaven.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Mar. 10. Vol. 76. No. 10. pp. 612–628. With 2 maps & 6 figs. on 2 plates.

Fadda (Siro). La malaria nelle colonie italiane dell'Africa Orientale.—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Feb. Vol. 17. No. 2. pp. 105–114. With 2 figs.

Barber (M. A.) & Rice (J. B.). **Malaria Studies in Greece. The Relation of Housing to Malaria in Certain Villages of East Macedonia.**—*Amer. Jl. Hyg.* 1935. Nov. Vol. 22. No. 3. pp. 512–538. With 4 figs.

It made no difference, in this region, whether the house was old and dark, or new and light. Only one thing mattered, and that was screening.

These observations were made in certain plains of Eastern Macedonia where *A. elutus* is the chief and, probably, the only important vector of malaria. *A. superpictus* is very uncommon and *A. maculipennis*, though abundant, is very rarely infected. The habits of sporozoite-infected *elutus* are the same as those of the uninfected. Infected *elutus* are found in stables nearly as often as in houses. Two different types of houses, the old and the new intermingled in the same village, were compared. The observations were continued for two years. With regard to density of anopheles, sporozoite rate, and human-positive percentage of blood meals, *elutus* in old and in new houses showed no significant difference. *Maculipennis* was more common in the old dark houses, but was very rarely infected. The proportion of infants infected was practically the same in both types of house. " The results on the whole do not offer much encouragement to the hope that improvement in housing, other than by screening, would be an effective anti-malaria measure. One could not even say that the house is the locus of infection, unless one includes in it the larger numbers of people sleeping outside." *W. F.*

Iraq, Government of : Ministry of Interior. Public Health Directorate. **A Compilation of Vital Statistics of Iraq 1935.** [**Malaria** pp. 19–24. With 1 folding map & 1 folding chart ; 32–35.]

The Public Health Adviser, Dr. T. B. Heggs, reports that malaria is the most important disease in Iraq. The spleen rate in the town of Baghdad is *nil*, but in the outlying country it is 30 per cent. In Basrah it is 17 per cent. in the spring and 40 per cent. in the autumn. Subtertian is the commonest form in lower Iraq, and benign tertian in middle Iraq ; quartan is limited to the hills of Kurdistan. The malaria season lasts from May to November, with a remission in September.

Owing to river floods, malaria was epidemic in 1926, 1929 and 1931. An average of 83 grains of quinine was issued to each of the 277,823 persons treated during 1934. *W. F.*

Kattan (H.). **Malaria in Palestine. 1911–1935.**—*Jl. Egyptian Med. Assoc.* 1935. Dec. Vol. 18. No. 12. pp. 802–813. With 3 charts.

The following figures represent the percentage of malaria cases among the patients attending :—

(1) Three years 1911–14	... ...	32 per cent.
(2) Three years 1914–17	... ...	47 ,,
(3) Five years 1919–23	... ...	19 ,,
(4) Five years 1923–28	... ...	9 ,,

W. F.

Schilling (Claus). Die Malariaepidemie auf Ceylon 1934/1935 nach den Berichten von Briercliffe und Gill.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Feb. Vol. 40. No. 2. pp. 51–63. With 1 fig.

Mauritius, Colony of : Annual Report on the Medical and Health Department 1st January to 31st December 1934 [Kirk (J. Balfour), Director]. Appendix III. pp. 53–56.— **Annual Report of the Malaria Branch for the Year 1934** [McGregor (Lewis J.), M.O. i/c Hookworm & Malaria Branch].

A drought which occurred early in the year 1934 was responsible for a reduction in the number of cases of malaria. The disease has shown a tendency to extend up into the healthy highlands, and the policy adopted during 1934 was to concentrate all efforts in the Planes Wilhems district which is situated in the centre of the island above the 600-foot contour. Work in the coastal lowlands was limited to the maintenance of existing drains, keeping them free from vegetation and the like. The spleen rate for the upland area investigated was 10·5, but, in spite of this, very few anopheline breeding places were found. The Malaria Officer is of opinion that the malaria in this area is the residuum of the outbreak which occurred as the result of the cyclone in 1931. All three types of malaria were found in almost equal proportion ; benign tertian being rather more common, and quartan rather less common than subtertian. *A. costalis* is much the most common mosquito, but *A. funestus* and *A. maculipennis* are also found.

W. F.

Bechuanaland Protectorate. Annual Medical and Sanitary Report for the Year 1934 [Dyke (H. W.), P.M.O.]. [**Malaria** pp. 12–17.]

Regular prophylactic quinine is recommended. Malaria occurs in cycles. An epidemic, following several healthy years and associated with famine, occurred in the Kalahari.

" Notwithstanding the disfavour with which quinine prophylaxis is regarded by many authorities, it is strongly advocated in this territory as being the only prophylactic available to the majority of the population. Some of the worst cases of malaria one has seen among Europeans recently have occurred in those who refused to take quinine because they had been

told, or read, that quinine in many malarious countries was now entirely discarded on the advice of eminent malariologists ! Whereas the experience in Ngamiland where malaria is endemic is that officials and others who take quinine regularly throughout the summer months are seldom incapacitated for their work even though when on journeys they were exposed to certain and unavoidable infection."

The incidence of malaria was very low from 1930 to 1934. During the latter year it remained low in the eastern part of the Protectorate, but in the western (Kalahari) part a very serious epidemic occurred. The resistance of the population " was lowered owing to lack of food, locusts having destroyed their cultivated crops . . . and because of foot-and-mouth disease they had been unable to export their cattle which is their normal source of income." The epidemic was preceded by heavy and continued rain. The case mortality was about 4 per cent. among Europeans and Eurafricans, and 10 per cent. among natives. There were many cerebral cases. As the affected districts lie some 200 miles from a railway-station, medical relief was carried by aeroplane. *W. F.*

CALONNE (R.). La malaria dans le Haut-Ituri. Le danger des eaux de barrages. [**Malaria in the High Ituri.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. Dec. 31. Vol. 15. No. 4. pp. 501–520. With 1 map.

An instance of man-made malaria at an elevation 5,000 feet, resulting from the damming of streams for agricultural purposes.

The High Ituri is on the west side of Lake Albert, facing Uganda on the opposite shore. It is a mountainous plateau lying at an altitude of some 5,000 or 6,000 feet and situated almost on the equator. The warm season begins in May and ends in October. When the rains come in September and October, fires are necessary even during the day. From January to April, when it is very dry, the days are warm but tempered by cool winds, and the nights are so cold that freezing point may be reached. The soil is very fertile and there are numerous plantations, especially coffee plantations. The author's examination of native tribes has convinced him that this region is normally almost free from malaria. The coffee-factories need water for the fermentation and decortication of the berries, and for this purpose dams have been erected across some of the ravines which have been converted into lakes covered with vegetation and sheltered from the wind. The splenic index of the labourers living in the neighbourhood of these reservoirs is between 80 and 90 per cent., as compared with 1 or 2 per cent. in villages more than 3 kilometres distant from them. The ravines are harmless in their natural state, but they are dangerous when they are disturbed. For example, several were cleared and imperfectly drained for agricultural purposes by a religious mission, with the result that malaria broke out among the children in their school. Two anopheles have been found on the high plateau of Ituri, *A. gambiae* and *A. christyi*. Most of the cases examined by the author were infected with *P. falciparum*, but *P. vivax* and *P. malariae* were also seen.

[NEWSTEAD and CARTER first described *A. christyi* under the name *Neocellia ? christyi*, n. sp. from a single specimen (♀) taken in Uganda by Dr. C. CHRISTY. They wrote that it was a very striking species, but that they could not, from the single specimen, be quite certain whether it was correctly placed in the genus *Neocellia*. (NEWSTEAD

and CARTER. *Ann. Trop. Med. & Parasit.* 1911. Vol. 5. pp. 238–240.)

EVANS in her book on "Anophelines of Tropical and South Africa" (1927) described *Anopheles christyi* at p. 41, placing it in the group *Neomyzomyia* Christophers (1924), and giving its distribution as Uganda and Kenya Colony. Under *Habits* she noted that "adults were found commonly indoors in Nairobi." SYMES writing in 1930 on *A. christyi* in Kenya (*Kenya & E. African Med. Jl.*, 1930, Vol. 7, pp. 2–11) said that it appeared to be definitely attracted to cattle and that it occurred in dwellings occasionally, but in very small numbers. [This discrepancy may have seasonal explanation ?] LEESON reported it from S. Rhodesia, but stated (*S. African Jl. Sci.*, 1927, Vol. 24, pp. 424–428) that its larvae were not taken in sufficient numbers for data to be recorded. SEYDEL (*Rev. Zool. Bot. Afr.*, 1929, Vol. 28, pp. 28–31) has reported it from the Kivu district and the volcanic region of the Virunga in the Belgian Congo.

It does not seem to have been definitely associated so far with malaria in Kenya, S. Rhodesia, or Uganda.] *W. F.*

WILSON (D. Bagster). **Rural Hyper-Endemic Malaria in Tanganyika Territory.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Apr. 8. Vol. 29. No. 6. pp. 583–618. With 10 figs. [25 refs.]

Malaria causes comparatively little illness in Africans living in a hyperendemic area.

This valuable study was made in two out-of-the-way villages, with a Bantu population, situated about 15 miles to the north-west of Tanga which is on the East African coast in the north of Tanganyika. It is an area of high endemicity and all babies are infected before they are 5 months old. The author concludes that, "while children suffer from malaria during the first 2 years of life, and a few die during the first few months, older children cannot be said so to suffer, and no evidence was obtained of any harmful effects from malaria during adult life."

Babies during the first month were fat, placid and in excellent condition with no parasites in their blood. A month or two later the picture was very different. The children were fretful, feverish and evidently ill and the haemoglobin had dropped from about 85 to 45 per cent. The spleen was enlarged as far as the umbilicus and there was a congestive condition of the lungs. The change was partly due to malaria and partly to grossly unsuitable food. This state persisted for a little more than 6 months, and then, except for the few cases which ended fatally, improvement began. The time of first infection with parasites was generally the second month, all the babies were infected by the fifth.

During the period of acute infestation, which lasts about 18 months, the average number of parasites was 7,800 per cmm., and counts of 20,000 were often met with. The number of parasites and the size of the enlarged spleen remained about the same for the first two years, but there was very little danger to life after the first 6 months, and the degree of anaemia became less before the parasites began to decrease in number. Gametocytes began to appear when the children were 6 to 12 months old, and reached their maximum at the end of the second year. "Infectivity becomes a characteristic of these children neither when they are immune, nor before they have acquired their

immunity, but when they are in process of the change-over to the immune state." Gametocytes were seldom seen in adults. During the third, fourth and fifth years, the children played and ran about as though nothing was the matter with them. They were all infected, but the concentration of parasites in the blood (" parasite infestation ") was lower and very irregular ; counts were sometimes as low as 50 per cmm., and sometimes as high as 10,000. During this period the spleen became smaller. The spleen rate between 2 and 10 years was 85 per cent. ; in adults it was 39 per cent. The infestation rate at the age of 5 was rarely above 1,500 per cmm., and thereafter it declined constantly until about the fourteenth year, when it reached 177 per cmm. The parasite rate fell to 68 per cent. at the tenth year, and to 45 in adult life. The author is of opinion that " inherited tolerance plays little part in the ultimate acquisition of immunity, for nearly all babies . . . suffered from intense infections. . . . Such inherited characteristics as do play any part in the immune process are rather of the nature of a power to acquire immunity."

P. falciparum was the dominant infection at all ages, but the other species (including *P. ovale*) were also present during the first few years of life, and more rarely later. The immunity acquired to *P. falciparum* was less complete than that acquired to other species. The general result of mosquito dissections was a gland infection of 12·2 per cent. but, just after the rains, this figure was much higher and the number of mosquitoes in the houses was greater. This increase of infectivity was followed, not preceded by, a higher average parasite count (infestation rate) in the population, and 3 months after the rains the gametocyte rate in children was double what it was before. *W. F.*

Schwetz (J.). Observations et recherches sur le paludisme dans le Congo belge. Note sur les groupes d'âge qui sont le plus gravement frappés par le paludisme dans les régions hyperendémiques de l'Afrique centrale. [**Malaria in the Belgian Congo and Drug Prophylaxis.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. Nos. 1 & 2. pp. 60–75 ; 146–152. With 3 charts. [24 refs.]

Immunity develops with age. The difficulties of drug prophylaxis. The author's earlier conclusions are confirmed by further research. *P. falciparum* is the commonest parasite. All the small children have many parasites in their blood, but, in adults, parasites can be found only in thick films. Fifty per cent. of the babies have crescents, but these are not found in adults. Quartan parasites are fairly common in infants, but they are rare after 10 years of age. *P. vivax* is also found in infants, but it disappears even earlier than *P. malariae*, and is rare after the third year.

The author has learnt from experience that drug prophylaxis is far more difficult to accomplish than is realized by those who have never practised among ignorant natives in the tropics. " The regular administration of drugs can be carried out only under the direct and permanent supervision of a European, and, moreover, a European who is alive to the importance of the work." His own experiments were carried out among school children.

He found that the results with 0·5 gram (7½ grains) of *Cinchona febrifuge Roche* were rather better than those with 0·25 gram of quinine

hydrochloride, and the cost less. When these doses were given daily over long periods, it was possible to reduce the parasite rate from 80 per cent. to about 20 per cent., but not lower. *W. F.*

MATTLET (G.) Le kapfura ou kafindo-findo. [**Kapfuro or Kafindo-Findo.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. Dec. 31. Vol. 15. No. 4. pp. 521–525.

This is really malaria.

When Tabora was occupied by the Belgians in 1917, there was an outbreak of cerebrospinal meningitis among the troops which, the white Fathers of the Mission maintained, was really a native disease known as Kafindo-findo. This disease, the Fathers said, was characterized by a membrane which formed at the base of the tongue ; in severe cases there ensued high fever, cerebral symptoms and sometimes death from suffocation. It could be cured by scratching the back of the tongue with a pointed stick, and the Reverend Fathers scratched and cured the natives in hundreds wherever the disease was rife among them. The author sought for many years to find typical cases of the disease. It is called Kapfura in Urundi. He was shown cases of rhinopharyngitis among missionaries who had been smoking strong native tobacco, and cases of pharyngeal catarrh from other causes. Eventually he heard of some cases at Ruhengeri, north-west of Ruanda, in marshy country full of streams and rushes, at an elevation of 6,000 feet. These cases had fever and they had also numerous subtertian parasites in their blood. The same was found in all the severe cases of Kapfura, and quinine has now removed the dread of this disease from the missions. The author thinks that malaria was introduced into the highlands by the troops passing through it during the war, but Europeans are unwilling to admit that it is really malaria, because they affirm that there is no malaria, on the plateau, and they sleep without mosquito nets to prove it. *W. F.*

RUSSELL (Paul F.). **Epidemiology of Malaria in the Philippines.**—*Amer. Jl. Public Health.* 1936. Jan. Vol. 26. No. 1. pp. 1–7. [24 refs.]

Malaria control is impracticable in many rural areas in the tropics, because it is too expensive.

Malaria is responsible for ten to twenty thousand deaths annually in a population of 13,000,000. There are probably about 2,000,000 cases a year. It does not occur in the large cities. About 60 per cent. of the infections are benign tertian, blackwater fever is very rare and malaria is not such a serious menace as it is in British or Dutch Malaya. Barber found a parasite index of 11 per cent. and a spleen index of 13·3 as the result of examinations made in 14 provinces.

The malaria mortality rates have fallen greatly in the last 30 years ; the rates were : in 1905, 662 per 100,000 ; in 1925, 218 ; in 1932, 77. There is no evidence that larval control, quinine consumption, or the use of bed-nets has been responsible to any extent for this improvement. Probably changed diagnosis has been a factor.

Two anopheles have been incriminated as vectors : *A. minimus* var. *flavirostris* and *A. maculatus*. The latter is zoophilous and rarely spreads malaria in the Philippines. *A. minimus*, the carrier, feeds with equal avidity on man and buffaloes ; it enters houses at night, but

is seldom found there in the day. Its effective range is rarely over one kilometre. It breeds in small clear streams and flowing irrigation ditches ; more often in shady than in open places. It is never found in rice fields, or above 2,000 feet altitude. Malaria is chiefly prevalent in the foothills where small streams offer breeding places suitable for this mosquito.

Paris green seems most suitable for combating malaria in the Philippines, and it has been used with success in army centres and on estates. Gambusia have been of no value at all. There is hope that malaria may be controlled, in those communities which can afford it, by the use of Paris green, but there are many districts in the Philippines which are too poor for this. " The longer one observes malaria in the tropics the more one is forced to conclude that, so far as average rural areas are concerned, the problem of control is still unsolved. Malaria prevention in the tropics by means of drains and subsoil pipes, larvicidal oil, and Paris green is entirely feasible . . . in cities, organized industrial and agricultural centers . . . ; but for most malarious rural areas in the tropics it appears that we have no economically feasible control methods . . . So far as I know, the drugs quinine, plasmochin and atabrine have never eradicated malaria from an area or even from a single town." *W. F.*

FARINAUD (M. E.). La lutte contre le paludisme dans les colonies françaises. [**Malaria and Antimalarial Measures in the French Colonies.**]—*Ann. de Méd. et de Pharm. Colon.* 1935. Oct.–Nov.–Dec. Vol. 33. No. 4. pp. 919–969.

The author surveys, in the first part of this paper, the conditions as regards malaria in the different French colonies and mandated territories ; in the second part, he discusses the methods adopted for its prevention. He considers it waste of time to begin with propaganda when dealing with backward races. First heal the sick, next protect the healthy, then educate. Prophylactic quinine has been taken for years in Africa, it prevents serious illness and death, although it does not prevent malaria. For individuals it is useful, but for collections of labour under ordinary conditions it is of little value ; for example, in the agricultural colony of Fri-Cu in Tonking, 30 per cent. of the children had parasites in their blood at the end of a year's prophylactic treatment. The results with plasmoquine and atebrin have been rather more promising ; in the case of benign tertian, prophylaxis with these drugs may merely render the infection latent, but in subtertian, as JAMES has shown, if the attack does not occur within the usual incubation period it means that the infection has been aborted. Unfortunately atebrin accumulates in the body and therefore it cannot be used with safety in small daily doses over a long period. Drug prophylaxis depends for its success not only on constant and close supervision, but also the community under treatment must be isolated, stable and under strict control ; every carrier must be treated. Even where mass prophylaxis has been successful, malaria quickly returns to its former level when the drugs are withdrawn. The best results appear to have been obtained with atebrin, and the author thinks it possible that rhodoquine and quinacrine the French forms of plasmoquine and atebrin may be used in the French colonies instead of quinine. At present between 7 and 8 tons of quinine are used annually in French possessions at a cost of more than 3 million francs a year. *W. F.*

Fréville (L. H.) & Nguyen-van-Luong. Quelques nouveaux cas de contaminations paludéennes au cours de pélerinages au mont Baden (Tayninh).— *Bull. Soc. Méd.-Chirurg. Indochine.* 1935. June. Vol. 13. No. 5. pp. 562–569.

Mickaniewski & Hai. Enquête sur le paludisme dans la province de Baria.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. June. Vol. 13. No. 5. pp. 543–557.

Ristorcelli. Note sur le paludisme dans la région de Tatahouine.— *Tunisie Méd.* 1936. Mar. Vol. 30. No. 3. pp. 119–122. With 3 figs.

Union of South Africa. Annual Report of the Department of Public Health for Year ended 30th June, 1935 [Thornton (E. N.), Secretary]. [**Malaria.—A. Control in Natal and Zululand. B. Tzaneen Field Station. C. Railway Areas** pp. 29–32. **Malaria** pp. 82–85.]

"We have been driven to employ hut-spraying during the malaria season as our main weapon over extensive sections of the country, and after a two-years' trial on the large scale are satisfied that the disease can be controlled by it in Natal and Zululand. It is essential, however, that (*a*) hut-spraying commence as soon as adult *gambia* or *funestus* begin to enter dwellings ; (*b*) it be applied to every habitation over the area to be dealt with, and that such area be as large as possible ; (*c*) every dwelling be thoroughly sprayed at least once weekly, but preferably bi-weekly . . . our method can only be successful when the vectors are in the habit of frequenting houses. Reduction in the infectivity rate may be very marked." It was below 1 in 1,000 of anopheles gorged with human blood in native areas formerly affected by malaria. This work was begun in 1932–33 with a pyrethrum insecticide. Many natives who were formerly hostile have now become convinced that malaria is associated with anopheles and they have begun to limit mosquito breeding by draining and restricted oiling. The author does not advise that complete reliance should be placed on insecticides alone in those closely settled communities where antilarval measures can be carried out ; but, over a large part of the country, and particularly in native reserves, antilarval measures are quite impracticable. The Railway Department put in 4,762 yards of subsoil drains and 13,000 yards of earth drains during 1934–35. During the winter dry season, arrangements were made to treat all relapse cases occurring in the native reserves. Municipalities and boroughs depended mainly on larval control supplemented in every case by spraying of dwellings with insecticides. On the coast north of Umfolosi, which is a highly malarious area, in accordance with Professor Swellengrebel's advice, no organized control measures were attempted lest they should tend to destroy the degree of natural immunity attained by the native population. Here there was no improvement in the malaria position during 1934–35, but elsewhere, " the results of measures taken are so striking that provided they are kept up we can count on a practical elimination of the disease in the country south of the Umhlatuzi River, in Zululand, and in the controlled area to the north of that river." In the coastal area, malarial incidence was much less than in previous seasons though there was little reduction in the numbers of *A. gambiae.*

Seepage areas are dealt with in some areas by planting trees to promote drying and absorption, natives have been induced to plant gum trees (*E. saligna*) and the Native Affairs Department has set aside an annual sum for the establishment of plantations. Screening of dwellings and public buildings is widely used. Monel metal is used by the Railway Administration in Natal, and bronze gauze in the Transvaal. [The insecticide employed is " Pyagra " diluted 1 in 17 with paraffin. See this *Bulletin*, 1935, Vol. 32, p. 393.] *W. F.*

SCHARFF (J. W.). **Anti-malarial Drainage from the Point of View of the Health Officer. Parts I & II.**—*Malayan Med. Jl.* 1935. Dec. Vol. 10. No. 4. pp. 119–137. With 15 figs. & 1 diagram.

" A practical knowledge of drainage technique is as necessary for malaria field-workers as is the study of mosquito ecology." This knowledge is not easy to come by, and, in this series of papers which deals with the theory and practice of anti-malaria drainage, the author has done great service to his fellow-workers in malarious countries. He emphasizes the need for proper control of general anti-mosquito and anti-malaria measures. It has happened far too often, he writes, that spasmodic efforts on the part of local authorities, while leading in some cases to partial success, fail in the end for lack of continuity, and bring discredit upon measures which would command success if well carried out. He first considers the different types of soil, the size of their particles, the air-space between the particles, and the influence of these factors upon permeability. Next, he discusses water in its relation to soil particles, and the water-table in its relation to the formation of springs and seepages. Drainage removes the excess of water from the soil, and the water is replaced by air. Subsequently, each fall of rain refills the " pore " spaces in the soil with water which in its turn again gives place to air. This phenomenon is the aeration of the soil, so important to agriculturists. Without this process of aeration, the organisms which convert the oxygen and nitrogen of the pore-spaces to the use of the plants cease to work ; the useful plants die and are replaced by weeds which are specially adapted to grow without soil-air. Drainage " sweetens " the soil, the farmer says ; in some places it removes the excess of alkali ; in others, it removes the excess of peaty acids. Drainage not only reduces the amount of malaria, but, at the same time, it enriches the land and the people. Filling is justified in places where, in addition to reclaiming a dangerous swamp, a great housing scheme is made possible ; but only under exceptional circumstances should filling be debited to an anti-malarial budget. Apart from such large schemes, the author does not recommend filling in the Malay States. The material employed is often impervious ; springs and seepages reappear on the top of the filling, and oozing water spreading over it continues to afford numerous breeding places for dangerous anopheles.

The second part of this paper deals with " The Principles and Objects of Land Drainage in Connection with Anti-Mosquito Projects." It begins with a description of the effect of drains upon the movement and level of the subsoil water. " Without water it is impossible to grow crops, but too much water may be as bad as too little. . . . Even wet rice cultivation forms no exception to this rule, and though such land must at certain seasons be flooded for the growth of a crop of rice, yet at other seasons surplus water must be removed in order to aerate the

soil. The reason for the inhibitory effect which this slowly alternating flooding and drying has on the breeding of malaria-carrying mosquitoes is not at present understood." The influence of geological features, such as the arrangement and permeability of the strata, on drainage is next discussed ; this is followed by a consideration of practical drainage problems such as the drainage of ponds, lakes and swamps, and examples are given of different methods which have been employed with success in dealing with special cases. For example, dangerous anopheles were found breeding in the puddles formed by the drippings from stand-pipes in Penang, where the surface layer of the soil is impervious with a pervious stratum underneath. Drainage was successfully accomplished by sinking a shaft with the bore-hole auger used in latrine construction, through the impervious layer into the pervious stratum beneath. This article which is illustrated with numerous diagrams and sketches will be continued in a later number. *W. F.*

Scharff (J. W.). **On a Method of planting and growing Grass in Connection with Anti-Malarial Drainage Projects.**—*Malayan Med. Jl.* 1935. Dec. Vol. 10. No. 4. p. 153.

One of the difficulties in draining hill land is to maintain the drained surface undamaged under frequent falls of rain. In the Malay States, grass has been found the best protection. The efficiency of anti-malarial drainage frequently depends upon the quickness with which grass plants can be induced to take firm hold upon the soil. It is necessary to plant a creeping grass to provide the necessary stability. A method used in the Dindings is as follows : Thin sods of grass are cut about 2 feet square ; they are rolled up like a jam-roll and chopped into small sections 1½ to 2 inches square. These are thrown into a barrel half full of a mixture of cow-dung and water which has been allowed to mature for at least 2 days. The mixture should have the consistency of thick porridge. The surface which requires turfing is beaten down quite flat and is plastered with a layer of the mixture about ½ an inch thick. On the following day it is watered, and, on the third day, blades of grass begin to appear. Avoid planting in stormy weather. Do not scythe the grass until 2 months later. *W. F.*

Rouché. Deux années de lutte contre les moustiques au centre d'aviation de Rochefort. [**Two Years' Antimosquito Work at the Rochefort Aviation Centre.**]—*Arch. Méd. et Pharm. Nav.* 1935. Oct.–Nov.–Dec. Vol. 125. No. 4. pp. 545–582. With 26 figs., 1 folding map & 2 plans.

Prevention of mosquito-nuisance by ordinary methods carried out with enthusiasm and success. Waste oil from the aeroplanes is used.

The naval aviation centre and school for army air mechanics is situated outside the town of Rochefort in a loop of the river Charente not far from its mouth. It is surrounded by flat, marshy land. The new buildings required in connexion with the aerodrome and school have interfered with the natural drainage which is difficult in any case owing to the flat, low-lying land. The breeding places of the mosquitoes are largely man-made ; for instance, a large stagnant pond in connexion with the electric light works. An enormous amount of culicine breeding takes place in sewage from water closets, latrines and septic tanks. Mosquitoes have been so numerous as to prevent sleep

at night. In days gone by, malaria was a serious disease in Rochefort and there are still a few cases every year. There were 22 cases between 1924 and 1928. They were all due to *P. vivax*. The author observed two cases in 1934. *A. maculipennis* var. *atroparvus* is found in the buildings ; they do not breed in the government aerodrome area, but in neighbouring farms situated in the marshes outside the camp. A great deal has evidently been accomplished in the way of filling up pools and cleaning up streams and drains.

Screening is provided in some of the barracks, and the dormitories are sprayed with insecticide. An almost unlimited supply of waste oil from the aeroplanes is available for spraying, and this is used in drip-tanks and sprayers. The results have been excellent, and in some places where mosquitoes were present in hundreds, there are now none. In the ditches of the farms, just outside the camp, anopheles continue to breed. *W. F.*

Sautet (Jacques). Cinq années de lutte antipaludique dans le nord de la Corse. [**Five Years' Antimalaria Work in North Corsica.**]—*Rev. Méd. et Hyg. Trop.* 1936. Jan.–Feb. Vol. 28. No. 1. pp. 23–30.

The anti-malaria service was inaugurated in 1930. The author was the Director of the work in the northern half of the island with headquarters at Bastia, and about 20 dispensaries scattered over the country. Mobile units visited the dispensaries, sought out the infected people, examined and card-indexed them and prescribed the treatment to be carried out locally with quinacrine or quinine, and rhodoquine. In rural districts, *Gambusia* were introduced into breeding places ; in populous centres, Paris green was employed. Supervisors on motor-bicycles covered large areas inspecting the work carried out by the labourers. The results were good during the first two years, but they were less good in 1934 and 1935 owing to an influx of Italians and other foreigners for employment on public works, and also because antilarval work had been suspended owing to lack of funds. *W. F.*

Balfour (M. C.). **Some Features of Malaria in Greece and Experience with its Control.**—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 2. pp. 114–131.

Drainage better than drugs Fewer relapses after atebrin than after quinine, but fewer relapses after atebrin plus plasmoquine than after atebrin alone.

Observations on malaria in Greece have been made, since 1930, in five principal " field study areas " which have been established in Attica, the Peloponnesus, Central Greece, Macedonia and Thrace. An important point which has been established is that natural fluctuations occur in malaria which varies from a mild endemic to a severe epidemic form. Meteorological conditions have the greatest influence in determining the situation. " The winter rains, and the snow which falls on the mountains, are the foundation upon which the following malaria season develops. . . . When a wet spring is superimposed on a wet winter . . . a bad malaria season will probably follow." *A.*

elutus is the most important vector, *A. superpictus* is also a dangerous carrier ; *A. maculipennis* is very numerous, but much less important. The average rates of infection with sporozoites during the 3 years were : *A. elutus* 1·29 per cent. ; *A. superpictus* 0·84 per cent. ; *A. maculipennis*, 0·07 per cent. The first two fly for long distances, up to 5 kilometres, and, at some places in central Greece it has been necessary to extend antilarval measures to a radius of 5½ kilometres (3¼ miles). New infections occur from the middle of May to the middle of October. In ordinary years, infections with each of the three types of parasite occur in equal proportion, but, in epidemic years, *P. falciparum* infections predominate. As regards the effects of malaria upon the population, in ordinary years, though the spleen index may be about 70 and the parasite rate about 30, there is very little illness, but in epidemic years every one suffers. " It is now recognized in Greece that quinine is a therapeutic and not a preventive measure. The use of quinine has been, and will continue for years to be, the backbone of relief for the majority of malarious communities." Comparative tests were made with quinine, atebrin, and plasmoquine 0·02 gram plus atebrin. The relapse rates were 45 per cent., 30 per cent. and 8 per cent. respectively. The author is of opinion that 10 days is the optimum duration of quinine treatment ; five days he considers too short. " The malaria worker soon arrives at the conclusion that in Greece, as elsewhere, drainage operations, large and small, are the basis of permanent antimalaria efforts. . . . In the Struma Valley . . . a drainage project, costing about $20,000,000, is also nearing completion." Drainage supplements and gradually takes the place of Paris green.

W. F.

Rice (E. Milford). **Observations on Malaria in Assam, with Special Reference to Cold Weather and Pre-Monsoon Anti-Larval Control.** —*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 371–388. With 4 graphs. [16 refs.]

Anti-larval measures in Assam should be carried out during the first half of the year instead of from March to November.

The period at present generally advocated for the application of anti-larval control is from March 15 to November 15. *A. minimus*, the only carrier, breeds in clear running water. On many estates the breeding area is limited to one or two small streams, and the breeding time is limited to the period January to June. When the monsoon breaks in June, these streams are flushed out with muddy water and breeding ceases. On some estates, breeding proceeds in the same way until the beginning of the monsoon, but, instead of coming to an end, it continues in monsoon streams, drains and other suitable places, with the result that the malaria season continues for a longer period. The author concludes that the breeding of *A. minimus* from early January to mid-June is the principal factor responsible for the incidence of malaria and that transmission in the cold weather is the cause of the April rise ; he suggests that anti-larval measures applied during this period would be more economical and efficient than those applied in accordance with present practice from mid-March to mid-November. Estates with no breeding places in their area have no malaria, though breeding may be taking place at a distance of a half to two miles. The usual flight distance of *A. minimus* is therefore not more than half a mile. *W. F.*

RICE (E. Milford). **Anti-Larval Oil Application by a "One Man" Brushing Method.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 499–500. With 2 figs. on 1 plate.

This is a modification of Quaife's brush method of oiling. The author attaches a bamboo brush to the nozzle of a Knapsack Solo Sprayer by means of two motor-car hose-pipe connexion fittings. The two operations, the application of the oil and its distribution with the brush, can therefore be carried out by one cooly instead of two. *W. F.*

WHITE (R. Senior). **Malaria Control by Subsoil Drainage at Waltair.**—*Records of the Malaria Survey of India.* 1936. Mar. Vol. 6. No. 1. pp. 13–18. With 5 figs. & 1 diagram on 2 plates.

Peasants object to Paris green on their paddy-fields.

For some years, earth drains and oiling were employed. Early in 1932 the conversion of the open drains into subsoil drains was begun. The drains were deepened to 3 feet, flat-sided stones were laid to form a tunnel over which smaller stones were placed, gradually decreasing in size towards the top. The whole was topped off with earth in which grass was planted. The subsoil drainage proved more efficient and was less costly than the open drains and oiling. On one side of the town there were 30 acres of paddy which was regularly dusted with Paris green. The peasants strongly objected to this, and, after the dusting had been going on for a year, they refused to let it continue. The land was eventually bought by a speculator for building purposes. *W. F.*

EJÉRCITO (Antonio). **Malaria and its Control in the Philippines.**—*Monthly Bull. Bureau of Health.* Manila. 1935. Aug. Vol. 15. No. 8. pp. 253–258.

Systematic larval control was begun in 1926, and Paris green was employed as a larvicide over an area with a radius of 1·5 kilometres (nearly a mile) around the communities to be protected. In some localities the results were good, but in others they were a failure, and it is suggested that the radius controlled was not extensive enough to prevent anopheles reaching the dwellings at the centre. After six years of Paris green control, this method has been abandoned except in certain places where money is available ; elsewhere, reliance is placed on the use of mosquito nets and the treatment of the sick. *W. F.*

WALCH (E. W.) & SOESILO (R.). **Malaria Control in the Netherlands Indies.**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1935. Vol. 24. No. 3. pp. 86–94. With 15 figs. (11 on 6 plates).

This paper was published in the Transactions of the 9th Congress of the Far Eastern Association of Tropical Medicine and Hygiene, and is summarized in this *Bulletin*, 1935, Vol. 32, pp. 728–29. The paper under review contains some good photographs and a picture of *Puntius javanicus*, the fish which feeds on pond vegetation. This note is inserted because the Dutch Journal is easier to obtain for reference than the Transactions of the Far Eastern Association. *W. F.*

Goldfeder (A. E.). Malaria und Auge. 4. Mitteilung: Ueber ein allgemein zugängliches Augensympton der chronischen und larvierten Malaria. [**Malaria and the Eye.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. May. Vol. 40. No. 5. pp. 207–211. With 3 figs.

A new eye symptom is described by the author in latent and chronic malaria.

In the protozoological Institute of the Ukrain the melanoflocculation reaction of Henry has been employed in the diagnosis of malaria and the author considers it possible that with improvements the reaction may become as specific for malaria as the Wassermann reaction for syphilis. As another comparatively easy method of diagnosis of malaria the author describes an eye symptom which can be readily recognized by the general practitioner. He describes it as "a symptom of malarial eye blood vessels." It consists of the presence of peculiar and unusual blood vessels in the conjunctiva of the eyeball. He describes and illustrates the appearance in detail. The changes generally occur in one eye but sometimes both eyes are affected. He describes his method of demonstrating the appearances. He considers that this eye symptom, which he describes, is as pathognomonic for malaria as Hutchinson's teeth are for congenital syphilis.

The vessels are superficial and in fact appear as if raised above the surface of the ocular conjunctiva, they are generally of larger calibre than the other conjunctival vessels, and though they vary in depth of colour they are always darker than the other surface vessels. If the eye is directed straight forwards the vessels have a wavy outline (spiral or corkscrew shaped), if the eye is moved to the opposite side they are drawn out like strings [*i.e.*, straightened] (Fig. 1); they do not divide dichotomously like other conjunctival vessels, but as they approach the sclero-corneal junction either divide, each into two running parallel

Fig. 1.

Fig. 2.

Unusual blood vessels in the conjunctiva of the eyeball, described by Goldfeder as pathognomonic for malaria.

[Reproduced from the *Archiv für Schiffs- und Tropen- Hygiene.*]

round the cornea, or, without dividing, turn sharply to run parallel with the corneal margin (Fig. 2) ; they do not anastomose with other vessels but are lost in the fornix of the conjunctiva.

To those specially interested the paper may be consulted in original and the figures therein studied. *E. D. W. Greig.*

Bhattacharjee (N. C.). **A Case of Malaria with Acute Mania.**—*Indian Med. Gaz.* 1935. Dec. Vol. 70. No. 12. p. 686.

A patient with subtertian malaria became so violent that it needed four men to hold him in bed. He talked nonsense, kept his eyes tightly closed and resisted all attempts to open them ; his temperature was between 99·4°F. and 101°F. He improved rapidly on quinine and in about 24 hours the symptoms had disappeared. *W. F.*

Grossman (J.) & Solomon (Eug.). Quatre cas de syndrome appendiculaire d'origine paludéenne. [**Four Cases with Symptoms of Appendicitis due to Malaria.**]—*Bull. et. Mém. Soc. Méd. Hôpit. de Bucarest.* 1936. Jan. Vol. 18. No. 1. pp. 10–18.

The authors review former observations of this condition and relate the history of their four cases. The signs which put them on the track of a correct diagnosis are leucopenia in a case resembling appendicitis, together with a good general condition and a pulse corresponding with the temperature. The presence of parasites greatly strengthens the diagnosis, but does not rule out appendicitis entirely. The symptoms disappear under quinine if they are due to malaria. *W. F.*

See also p. 369, Yenikomshian, **Septicaemic Plague simulating Malaria.**

Thomas (W. L.) & Keys (S.). **Accidental Transmission of Malaria by Blood Transfusion. With a Note by** S. C. Dyke.—*Lancet.* 1936. Mar. 7. pp. 536–537. [12 refs.]

Transfusion with citrated blood by means of a three-way syringe was performed on August 24th and September 9th, 1935. Eighteen ounces of blood were inoculated on the first occasion and ten on the second. On September 12th, the recipient developed a high intermittent fever with rigors. On September 19th, the blood was examined for malaria parasites and *P. vivax* was found. The donor had served as a soldier in India from 1927 to November 1933. No parasites were found in his blood and he had never, so far as he knew, suffered from malaria, but in June 1934, he had had a short series of shivering attacks each lasting 2 or 3 days. *W. F.*

Day (L. F.). **Quinine and Otosclerosis.**—*Malayan Med. Jl.* 1936. Mar. Vol. 11. No. 1. pp. 53–54.

The author describes 3 cases of otosclerosis which began with progressive deafness and tinnitus following a course of quinine treatment. Two of the patients were schoolmasters, one 28 and the other 25 years old, who could not hear a speaking voice more than 3 or 4 feet away. The third patient was a Chinese shopkeeper aged 45. It is suggested that the deafness was due to the effects of the hyperaemia produced by large doses of quinine. This causes absorption of circumscribed areas

of bone around the labyrinth, which are later replaced by new spongy bone. When once the bony changes of otosclerosis have begun, they progress. Eventually the stapes becomes ankylosed to the oval window and the bony changes spread to the cochlear region ; degeneration of the auditory nerve follows. *W. F.*

Dang (Mi-Gieu), Hemenway (Ruth V.) & Lau (Stephen). Report of Nine Hundred and Sixty Cases of Malaria in Mintsing, Fukien.—*Chinese Med. Jl.* 1935. Nov. Vol. 49. No. 11. pp. 1235–1240.

Yui (E. M.) & Paty (R. M.), Jr. A Review of 203 Malaria Cases.—*Chinese Med. Jl.* 1935. Nov. Vol. 49. No. 11. pp. 1228–1234.

Sicault (H.) & Nesserlin (H.). Observations de quelques cas de néphrite quartane avec syndrome de rétention chlorurée.—*Bull. Soc. Path. Exot.* 1936. Mar. 11. Vol. 29. No. 3. pp. 268–274. [16 refs.]

Zimine (E.). Un cas de pleurésie hémorragique d'origine paludéenne.—*Bull. Soc. Path. Exot.* 1936. Mar. 11. Vol. 29. No. 3. pp. 267–268.

Rankov (M.). Die Verteilung des *Plasmodium vivax* und *Plasmodium immaculatum* bei verschiedenen Altersgruppen. [**Distribution of *Plasmodium vivax* and *immaculatum* in Different Age Periods.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. July. Vol. 40. No. 7. pp. 277–289. With 14 figs.

The author made his observations in southern Jugoslavia in 1924. He examined in all 442 cases of which 44 per cent. were benign and 56 per cent. malignant tertian malaria. He studied the distribution of the infections in the various age periods and his paper is illustrated with diagrams and tables.

He concludes that the percentage distribution of benign and malignant infections in the age groups in southern Jugoslavia is markedly different. There is a quite regular fall in the percentage of benign tertian with increasing age and a corresponding increase of malignant tertian. He thinks the explanation of this phenomenon lies in the different speed and degree of development of the resistance of the organism. *E. D. W. Greig.*

Pandit (S. R.). **The Morphology of Malarial Parasites.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 389–392. With 63 coloured figs. on 2 plates.

Thin films were exposed to the vapour of osmic acid, while they were still wet, by inverting the slide over the open mouth of a bottle containing a 2 per cent. solution of osmium tetroxide in 1 per cent. chromic acid. The films were fixed in methyl alcohol and stained with Giemsa. Coloured plates are given in which such preparations are compared with ordinary air-dried films. " It is suggested that fixation of wet films over the vapour of osmic acid gives a truer picture of the parasites." *W. F.*

IVANIĆ (Momčilo). Ein neuer Beweis für den ursprünglich promitotischen Charakter der Kernteilung beim Tertianaparasiten (*Plasmodium vivax* Grassi et Feletti). [**Fresh Proof of the Primitive Promitotic Character of Nuclear Division in** *Plasmodium vivax*.] —*Zent. f. Bakt.* I. Abt. Orig. 1936. Feb. 13. Vol. 136. No. 1/2. pp. 109–111. With 1 fig.

The title describes the nature of this communication. The author obtained his material for investigation from a 10-year-old-boy who was very heavily infected with benign tertian malaria. The blood films were stained by Giemsa's solution ; [method of fixation is not mentioned].

He concludes that the nuclear division occurring during the schizogony phase of the *Plasmodium vivax* is promitotic in character and, probably, this character is common in this parasite. From this he holds that a new support has been found for the view that the malaria parasite arises from a lower rhizopod which regularly divides by promitosis, hence it appears that malaria infection originally took place by oral ingestion, which makes the mosquito theory questionable. *E. D. W. Greig.*

IVANIĆ (Momčilo). Ein neuer Beitrag zur Kenntnis der Kernteilung beim Tertianaparasiten (*Plasmodium vivax* Grassi et Feletti). [**Nuclear Division in** *Plasmodium vivax*.]—*Zent. f. Bakt.* I. Abt. Orig. 1936. June 12. Vol. 136. No. 7/8. pp. 418–420. With 2 figs.

A study of nuclear division in *Plasmodium vivax*.

The author refers to his previous communication dealing with this subject and the present paper is a continuation of the investigation. Two mitotic nuclear division stages of *Plasmodium vivax*, one early the other late, are described. He states that he again produces proof that the original promitosis of *Plasmodium vivax* changes into a true mitosis. *E. D. W. Greig.*

LINTWARÉFF (J. J.). Beiträge zum Studium der Malaria-pathogenese. [**Study of the Pathogenesis of Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Feb. Vol. 40. No. 2. pp. 63–73.

A study of the part played by haemoglobin in the pathogenesis of malaria.

The author refers to his work on the significance of haemoglobin in pathology. He considers that the toxin formed by the malaria parasite is adsorbed by haemoglobin of the red cells, and passes into the blood plasma. The haemoglobin combined with the malaria antigen circulating in the blood stream causes a hyperplasia of the reticulo-endothelial tissue, especially that in the lungs and mesentery, whereby the antigen in this tissue becomes transformed into malarial antibodies. He suggests that this hyperplasia and hyperfunction of the reticulo-endothelial tissue explains the beneficial effect of malariatherapy in metaluetic diseases, the RE tissue produces not only anti-malarial but also anti-syphilitic bodies. The haemoglobin-toxin is taken up by the cells of the renal tubules causing cloudy swelling (nephrosis) ; the iron from the disintegrated haemoglobin gives a beautiful Berlin blue reaction in the renal cortex. The haemoglobin-toxin also attacks the intima of the blood vessels in the mucous membrane of the intestinal canal producing thrombosis of the small vessels, resulting in necrotic lesions in the large and small intestines. By the action of the toxin on the walls of the small veins leakage occurs, resulting in numerous

extravasations in the pleura, peritoneum, epicardium and brain; these are usually minute, but at times larger haematomas take place.

E. D. W. Greig.

Jacobsthal (E.). Die Infektion der Reticulocyten durch Malariaplasmodien. [**Infection of Reticulocytes with Malaria Parasites.**] —*Klin. Woch.* 1936. June 27. Vol. 15. No. 26. p. 942.

Description of simple stain for reticulocytes and of the results obtained with it in malarial infections.

The author's stain is a modification of the Hirschfeld method. The procedure, which is very simple and easily applicable in practice, is as follows :—Blood films are stained with Loeffler blue (2–3 minutes), at the end of this time they are well washed in water, then stained 5–15 minutes in ordinary dilution of Giemsa. Washed in distilled water and dried in air. Fixation after Loeffler with saturated watery solution of perchloride of mercury may be employed; although finer results are obtained with unfixed films, the latter are not so good for permanent preparations as the fixed films.

Employing the above technique the author found that in infections with *Plasmodium vivax* and *falciparum* the parasites selected the young red cells; 90 to 98 per cent. of infected cells were reticulocytes. This he considers of considerable clinical importance as a number of these young red cells are destroyed and so anaemia is produced. He also noticed that the reticular structure of infected reticulocytes was altered. He stresses the point that to get good results the films must be fresh.

E. D. W. Greig.

Sarkissiane (A. B.). La moucheture de Schüffner et le ponctuage de Maurer dans les erythrocytes dans les cas de leur coloriage par le nilblausulfate-azur-éozine.—*Folia Haematologica.* 1936. Feb. Vol. 54. No. 2/3. pp. 145–149. With 2 figs.

Sicé (A.) & Robin (Ch.). A propos du *Plasmodium falciparum* et de ses formes atypiques.—*Marseille-Méd.* 1936. Feb. 5. Vol. 73. No. 4. pp. 137–139.

Boyd (Mark F.), Stratman-Thomas (W. K.) & Muench (Hugo). **The Occurrence of Gametocytes of *Plasmodium vivax* during the Primary Attack.**—*Amer. Jl. Trop. Med.* 1936. Mar. Vol. 16. No. 2. pp. 133–138.

"A tertian malaria patient with an attack of average duration or better is almost certain to be highly infectious for anophelines at some time during his attack."

Gametocytes were invariably found at some time during the disease when its duration exceeded 16 days. Parasites rarely appeared earlier than the 10th day after inoculation by mosquitoes. Gametocytes were seen occasionally on the first occasion that the blood was positive, but never earlier than the 14th day after inoculation. Subsequently, gametocytes were produced in showers which occurred at regular 5-day intervals, on the 19th, 24th, 29th, 34th and 44th days. None was observed on the 39th day.

W. F.

DE ALDA CALLEJA (M.). Estado actual de los estudios sobre sueroflocuIación en el paludismo. (Reacción de Henry.) [**Present Views on Henry's Reaction in Malaria.**]—*Medicina Países Cálidos.* Madrid. 1936. May. Vol. 9. No. 5. pp. 203–236. With 5 figs. [104 refs.]

The author describes Henry's original reaction and subsequent modifications of it, the technique of its performance, sources of error, interpretation of results, records of previous investigators, and the value of the reaction in clinical practice, diagnostically, prognostically and as evaluating the results of treatment.

He sums up the present position as follows :—

1. Henry's reaction is a valuable aid in diagnosis of malaria, provided the deviser's instructions are followed.

2. It is of service in gauging the progress in the course of treatment, if a series of curves be plotted, and these curves are also useful in indicating relapse.

3. In the invasion stage, after accessions of fever, the reaction is positive in 100 per cent. ; in chronic malaria, results recorded have been varying, but with a high percentage positive.

4. The modified reaction is simple and consequently of use in clinics and in epidemiological studies.

5. The pH has but little influence on the reaction.

6. The proportion of non-malaria patients, such as syphilitic, tuberculous and leukaemic, reacting is small, but a positive result is sometimes obtained in protozoal infections, such as kala azar.

There is an extensive bibliography. *H. H. S.*

GNOCHVILI (I.), KEIGUELOUKHES (I.) & MOURGIRI (M.). La réaction Henry dans le diagnostic du paludisme. [**Henry's Reaction in Diagnosis of Malaria.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 6. [In Russian pp. 458–461. French summary p. 461.]

The authors carried out the melanoflocculation test on patients at the Institute of Tropical Medicine of Georgia. They tested 259 cases of malaria, 225 with other diseases and 27 healthy subjects. The reaction was positive in 95 per cent. of the first group, in 10·6 per cent. of the second, but was negative in all those in health. *H. H. S.*

WERNER (H.). Ueber die serologische Vervollkommnung der Malariadiagnose. Seroflokkulation.—*Deut. Med. Woch.* 1936. Feb. 28. Vol. 62. No. 9. pp. 347–350. [11 refs.]

PRUDHOMME (R. O.). Floculation des sérums dans l'eau distillée et réaction de Henry. [**The Flocculation of Serums in Distilled Water and Henry's Reaction.**]—*C. R. Soc. Biol.* 1935. Vol. 120. No. 38. pp. 944–946.

The substance which is flocculated by Henry's melanine is the same as the substance flocculated by distilled water in " surfloculance." It is present in all serums, but is increased in malaria.

In Henry's reaction : to the serum, diluted 1 in 5 with distilled water, melanine is added to the first tube and formol to the second which serves as the control. In a " surfloculant " serum, flocculation occurs in the distilled water control. If, in such a serum, one separates, by centrifuging, the floccules appearing in the distilled water tube, redissolves them in the same quantity of normal saline and then applies

Henry's reaction, the result is positive. If the supernatant fluid from the centrifuge be tested, it is found to be no longer positive. If a serum be examined which gives a precipitate in the melanine, but not in the distilled water control tube, it will be found that flocculation will occur in the latter when more distilled water is added ; say, to 1 in 10, instead of 1 in 5. If this precipitate be centrifuged off and dissolved in saline to a dilution corresponding to the original 1 in 5, it will give a positive Henry's reaction. With normal sera, negative to Henry's reaction, flocculation will not occur when one dilutes with distilled water up to 1 in 10, or so, but if one dilutes up to 1 in 40, or more, flocculation appears. If this substance, precipitated from normal serum by distilled water, be centrifuged off and redissolved in a small quantity of salt solution, this solution will give a positive result with Henry's melanine. The author concludes that a malarial serum differs from a normal serum only by reason of its greater content of a substance which is precipitable by distilled water. When this substance is present in great quantity, the serum is " surfloculant " ; *i.e.*, flocculation occurs in 1 in 5 of distilled water. When it is present in smaller quantity, flocculation is rendered macroscopically evident, at this dilution, only in the presence of an indicator such as carmine or Henry's melanine. This substance is normally present in all sera, and it is not surprising to find all grades between a normal serum, in which precipitation occurs only when a large quantity of distilled water is added, and a malarial serum in which precipitation occurs on the addition of very little. *W. F.*

Trensz (F.). Sur les différences d'activité que présentent la mélanine, l'eau distillée et différents indicateurs, dans la réaction de Henry. [**Differences in Activity displayed by Melanin, Distilled Water and Various Indicators in Henry's Reaction.**]—*C. R. Soc. Biol.* 1936. Vol. 122. No. 21. pp. 666–668.

In a previous communication the author adduced evidence showing that in Henry's reaction the melanin unites with a fraction of euglobulin to form a flocculating compound. He now shows that this melanin-euglobulin flocculum, unlike the flocculum produced by distilled water or 0·3 per cent. NaCl solution, is insoluble in 0·9 per cent. NaCl solution. Melanin is not an inert substance as are certain coloured pH indicators, for example, which disclose the existence of a state of things without influencing it. Melanin, on the contrary, intervenes actively in certain conditions of instability producing precipitation : it acts as a reagent. Its colour would be of no significance or interest were it not for photometric methods of examination.

Henry's reaction was carried out in the case of 57 malaria patients, comparing the action of melanin, albuminate of iron and saccharate of iron with the action of various coloured indicators and dyes :—carmine, indigo-carmine, diamantfuchsin, phenol sulphophthalein, methylene blue, methyl orange, thymol-sulphophthalein, gentian violet, dahlia violet, methyl orange III, Bengal red, bromo-thymol blue, bromo-cresol purple, rosaniline, Bismarck brown, toluidine blue, crystal violet. Melanin and the iron salts alone exhibited flocculating properties. The saccharate of iron is very active but difficult to titrate. The indicators and dyes used were found to be completely inert. [See also this *Bulletin, ante*, pp. 266–267.] *Norman White.*

Benhamou (Ed.) & Gille (R.). Les facteurs chimiques de la malaria-floculation (réaction de Henry) dans le paludisme anophélien. [**The Chemical Factors of Henry's Reaction.**]—*C. R. Soc. Biol.* 1935. Vol. 120. No. 40. pp. 1259–1261.

Analysis of the serum in malaria shows an increase of euglobulin and a decrease of serum-albumen and cholesterin. Henry's reaction is dependent upon the quantitative relation of these three substances to one another. The authors express this relation as a fraction, $\frac{\text{euglobulin}}{\text{serum albumen} \times \text{cholesterin}}$, which they term the "index of flocculability." In normal blood this equals from 0·01 to 0·05 and Henry's reaction is negative; when it is above 0·1 Henry's reaction becomes positive. For example, the index in a case of benign tertian was $\frac{\text{euglobulin } 4{\cdot}5}{\text{serum albumen } 23 \times \text{cholesterin } 0{\cdot}75} = 0{\cdot}26$, and Henry's reaction was positive. After treatment with quinine the index was $\frac{\text{euglobulin } 3}{\text{serum albumen } 49 \times \text{cholesterin } 1{\cdot}5} = 0{\cdot}04$, and Henry's reaction was negative.

W. F.

Villain (G.) & Dupoux (R.). Contribution à l'étude sérologique du paludisme. (Première note.) Préparation d'une mélanine artificielle (M. A.) et principe de son application à la réaction floculante de Henry. [**Henry's Reaction. Preparation of an Artificial Melanin. (M.A.)**]—*Bull. Soc. Path. Exot.* 1935. Dec. 11. Vol. 28. No. 10. pp. 915–921.

Introduce successively into a dry flask :—

Tyrosine Poulenc	0·30 gram.
Perchlorure de fer (*solut. officinale*)	0·40 cc.
Eau oxygénée 12 *vol.*	10·00 ,,
Eau distillée	10·00 ,,

Plug with cotton and shake. Leave for 15 minutes. Bring slowly to the boil and boil quietly for 1 minute. Pour the hot liquid into a 250 cc. flask containing 180 cc. of boiled, distilled water which is still hot, and boil quietly for 3 minutes.

Cool the flask rapidly under the tap.

After 30 minutes, add 3·20 cc. of N/1 caustic soda.

Leave for 12 hours at the temperature of the laboratory, and filter through a moistened paper.

The dark brown filtrate is the M.A.

It behaves in almost exactly the same way as Henry's melanine.

W. F.

Villain (G.) & Dupoux (R.). Contribution à l'étude sérologique du paludisme. (Deuxième note.) Technique de la M.A. floculation. (Troisième note.) Résultats obtenus dans la pratique de la M.A. floculation et conclusions. [**The Serology of Malaria. Tests with Artificial Melanin.**]—*Bull. Soc. Path. Exot.* 1936. Feb. 12. Vol. 29. No. 2. pp. 121–124; 124–130.

The authors describe the technique of their modification of Henry's reaction with the use of an artificial melanin which they call M.A. (see above). They conclude that the results with M.A. and with Henry's ox-melanin are approximately the same; they suggest that

their method should be substituted for the original, more complicated, procedure in out-stations, and should be used as a confirmatory test in central well-equipped laboratories. They found the reaction positive, apart from malaria, in kala-azar, typhus fever and typhoid fever. Doubtful reactions occurred in syphilitics and in recruits undergoing prophylactic inoculations. *W. F.*

Trensz (F.). Etudes expérimentales sur le rôle des euglobulines dans le mécanisme de la mélanofloculation de Henry. [**Euglobulins in Henry's Reaction.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. Dec. Vol. 13. No. 4. pp. 513–565. [63 refs.]

The author describes a series of experiments which he has carried out, and from which he concludes that Henry's reaction is due to qualitative changes in the euglobulin of the serum.

The serum-albumen and serum-globulin are increased in the experimental trypanosomiasis of rabbits. The globulins are not only increased but they become unbalanced, and their instability is shown by an increase in the euglobulins. Melanofloculation becomes positive as the euglobulins increase, and, as the rabbits improve under treatment, the instability of the serum disappears. Chorine and Gillier obtained positive reactions in normal serums to which normal euglobulin had been added. This experiment was repeated by the author, who states that the flocculation thus obtained is not a true flocculation, but has only the character of the surflocculation which occurs with distilled water. Normal euglobulin has much less affinity for melanin than the altered euglobulin which is present in malaria. Melanin becomes fixed to this special euglobulin and precipitates it.

The author obtained a characteristic positive reaction in 0·9 per cent. saline to which euglobulin from a case of malaria had been added. The reaction was not given by the other constituents of the serum. When the lipoid fraction of the euglobulin was removed by acetone, the euglobulin was no longer precipitated by melanin. The abnormal structure of the euglobulins in malaria is probably imparted to them by the cells in certain parts of the reticulo-endothelial system. Melanofloculation is not produced by the distilled water, for one can obtain it in undiluted serum. Distilled water is a bad medium for the melanoreaction because it precipitates, in addition to the euglobulins, lipoid and protein fractions which play no part in the true Henry's reaction.

W. F.

Canciulesco (M.) & Hirsch (R.). Sur la valeur diagnostique du pigment paludéen. Les épreuves de sa concentration dans le sang et dans les urines.—*Bull. Acad. Méd. Roumanie.* Bucharest. 1936. 1st Year. Vol. 1. No. 1. pp. 31–34. [10 refs.]

Daléas (Pierre) & Lavergne (Jean). Contribution à l'étude du paludisme congénital par la pratique systématique de la réaction de Henry et l'étude des formules leucocytaires chez les accouchées et leurs nouveau-nés. [**Congenital Malaria and Henry's Reaction.**] —*Bull. Acad. Méd.* 1936. Feb. 25. 100th Year. 3rd Ser. Vol. 115. No. 8. pp. 345–354.

Parasites were found in 3 cases out of 887, both in the mother and in the umbilical cord of the infant. In 10 cases, parasites were found in

the mother but not in the child. Henry's reaction was positive in 28 infants ; in half of these the mother's blood gave a positive reaction and in half it did not. In 27 cases the mother's blood was positive and the child's was negative. *W. F.*

RAYNAL (J.) La mélano-floculation (réaction de Henry au Tonkin). [**Henry's Reaction Tests at Tonking.**]—*Bull Soc. Méd.-Chirurg. Indochine.* 1935. Dec. Vol. 13. No. 10. pp. 1661–1700. [108 refs.]

This is a review of the literature, and gives the results of the test at Hanoi which do not differ from those elsewhere. *W. F.*

RAYNAL (J.). La réaction de Henry au Tonkin. Résultats de 853 mélano-floculations.—*Bull. Soc. Path. Exot.* 1936. Jan. 8. Vol. 29. No. 1. pp. 75–82.

MEERSSEMAN (F.) & LAFUMA (J.). Floculation spécifique et floculation banale dans la réaction de Henry. Intérêt des lectures photométriques en eau salée.—*C. R. Soc. Biol.* 1936. Vol. 121. No. 1. pp. 54–56.

MEERSSEMAN (F.) & LAFUMA (J.). Le contrôle sérologique du traitement antipalustre par la réaction de Henry.—*C. R. Soc. Biol.* 1936. Vol. 121. No. 1. pp. 52–54.

TRENSZ (F.). Lipoïdes et mélanofloculation de Henry.—*C. R. Soc. Biol.* 1935. Vol. 120. No. 40. pp. 1268–1270.

LIVIERATO (S. G.) & SALATA (C. Ch.). Recherches biologiques pour le diagnostic du paludisme latent.—*Acta Med. Scandinavica.* 1935. Vol. 87. No. 3–4. pp. 189–212. [26 refs.]

GOOSMANN (Charles). Dark-Field Illumination in the Diagnosis of Tuberculosis and Malaria.—*Jl. Lab. & Clin. Med.* 1936. Jan. Vol. 21. No. 4. pp. 421–424. With 5 figs.

REHDE (Rudolf). Ein Ueberblick ueber die Entwicklung der Malariaprophylaxe durch Arzneimittel. [**The History of Malaria Prophylaxis by Drugs.**] [Inaugural Dissertation.]—Reprinted from *Ergebnisse d. inneren Med. u. Kinderheilkunde.* 1935. Vol. 49. No. 89. pp. 64–121. With 9 figs. [201 refs.]

This is a thesis for the degree of Doctor at Kiel University. The author arranges his material under the headings : quinine from its introduction to Europe (1640) to 1880, the year of LAVERAN's discovery; quinine prophylaxis by various methods from 1880 to 1914 ; quinine prophylaxis in the war years and after ; the new synthetic remedies, plasmoquine and atebrin. There are 120 references for quinine and 50 for the newer drugs. Naturally German contributions receive the bulk of attention, *e.g.*, the methods of quinine administration are discussed under the names, PLEHN, ZIEMANN, KOCH and NOCHT. The general conclusion reached is that absolute protection is not obtainable by any method, but the chief reason for this, *viz.*, the failure of quinine to kill the sporozoites introduced by the mosquito, as YORKE and MACFIE showed, is mentioned only in the plasmoquine section.

Many interesting observations are collected and we learn that Robert Koch, a protagonist of quinine prophylaxis, did not himself practise it in Africa. As an illustration of the difficulty of getting quinine really taken, Ruge cited merchant ships where quinine was served out with rum: the rum was swallowed, the quinine went overboard. Many accounts of the use of quinine for prophylaxis are rendered worthless by the doubt whether the drug was really taken and absorbed.

A sufficient account is given of the introduction and early work on the use of plasmoquine and atebrin; here Germany takes the lead by right. Those who read German will find a great number of observations on the use of quinine collected here, but how far these are comparable remains uncertain; the snags are numerous. *A. G. Bagshawe.*

Henry (T. A.). **The Chemotherapy of Malaria.**—Reprinted from *Jl. Soc. Chem. Indust.* 1936. May 1. Vol. 55. No. 18. pp. 111T–117T. [31 refs.]

This is a review devoted to the correlation of antimalarial action, as measured in bird-malaria, with variation in chemical structure in the three principal types of antimalarial drugs, *viz.*, the cinchona alkaloids, plasmoquine and atebrin. It is shown that quantitative expressions for antimalarial action are not always strictly comparable owing to variations in technique, difference in standards and variations in the birds used, but in spite of these difficulties, a surprising amount of agreement is to be found in the assessment by different observers of antimalarial value throughout the same or similar series of compounds. Thus both the French (Fourneau *et al.*) and the Russian (Magidson *et al.*) teams of workers are agreed as to the dystherapeutic effect of increasing the weight of the alkoxy-group (R-O-) in position 6 of compounds of the plasmoquine type which may be represented by the condensed general formula*

$$R\text{-}O\text{-}C_9H_5N[\text{-}NH\text{-}(CH_2)_n\text{-}N(C_2H_5)_2]$$

They are also agreed as to the curious alternating effect of increasing the value of n in the basic side-chain of these compounds. The activity increases to a maximum with increase in the value of n up to $n=9$ after which it falls off, but the peaks at the odd numbers, $n=3, 5, 7$, are higher than those at the even numbers, $n=2, 4, 6$. Less work has been published regarding the acridine series of antimalarials to which atebrin belongs and which may be represented by the general formula $R\text{-}O\text{-}C_{13}H_6NCl\,[NH\text{-}(CH_2)_n\text{-}N(C_2H_5)_2]$. In this set antimalarial activity increases with rise in the value of n up to $n=4$ and then diminishes, which is the normal behaviour of items in a homologous series.

In the cinchona alkaloid group the most interesting points dealt with are the inhibition of anti-malarial activity (*a*) by the formation of an ether-oxide link between the central -CHOH group and the $-C_2H_4-$ side chain as in β-*iso*quinidine (see formula 2 below) and (*b*) by optical inversion at the -CHOH- group as in *epi*quinidine. Thus taking quinidine as a starting point and using Qn and Qdn to represent the quinoline and quinuclidine halves respectively of the molecule, the following remarkable changes in antimalarial activity result from the

* Complete diagrammatic formulae for this and other types of drugs referred to have been given already [this *Bulletin*, 1935, Vol. 32, p. 385].

slight chemical and physical changes (direction of optical rotation at -CHOH shown in [ ]) indicated.

1. Quinidine. CH_3O-Qn-CHOH-Qdn-$CH=CH_2$. [CHOH,+] Active.
2. β-*iso*Quinidine. CH_3O-Qn-CHO-Qdn-CH-CH_3. [CHOH,+] Inactive.
3. *epi*Qunindine. CH_3O-Qn-CHOH-Qdn-$CH=CH_2$. [CHOH,−] Inactive.

It is, however, not merely negative optical rotation at the -CHOH group which determines antimalarial inaction because quinine, the most active of all the cinchona alkaloids is laevorotatory at that point, and a consideration of all the results indicates that although a particular type of structure may appear to be associated with specific action, it is the combination of chemical and physical properties determined by that structure which is effective and any change in that structure producing an alteration in chemical or physical properties or both, may well inhibit antimalarial action. *T. A. Henry.*

Rosa (Alberto) & Valli (Enea Suzzi). L'atebrin e la plasmochina nella bonifica umana antimalarica. [**Atebrin and Plasmoquine as Malaria Prophylactics.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 1. pp. 32–59. With 3 figs. (2 maps). French summary.

The term " human bonification " here implies intensive treatment of persons before the usual annual outbreak of malaria in two highly malarious zones of Basso Ferrarese—S. Giuseppe and Gorino. The author describes the geographical position, the economic condition, and the malaria prevalence of these places. In S. Giuseppe of 1,620 inhabitants the splenic index was 28·4 and the malaria incidence 30·1 per cent. In Gorino among 83 children examined the splenic index was 21·6. The general plan of treatment was to give atebrin daily for 5 days and then, after an interval of 3–6 days, 3 days' course of plasmoquine ; atebrin 0·1 gm. and plasmoquine 0·01 gm. per tablet. The dosage was one tablet up to 4 years, two for those between 4 and 8, for those over this 3 tablets. During the summer quinoplasmine was given, 10 days drug, repeated after a 10-day interval, in dosage of 0·9 gm. sulphate of quinine and 0·03 gm. plasmoquine for 3 days and 0·6 gm. and 0·02 gm. respectively for the other 7 days, for adults. The incidence of malaria was considerably below that of the previous year : In S. Giuseppe from 30·1 in 1933 to 5·1 in 1934 and in Gorino with 500 inhabitants from 30·9 to 18·7 per cent. [in another place the last figure is given as 17·8]. *H. H. S.*

Kröber (Friedrich). Erfahrungen mit Atebrin, per os zur Prophylaxe, per injectionem zur Behandlung der Malaria. [**Atebrin by Mouth for Prophylaxis and by Injection for the Treatment of Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Mar. Vol. 40. No. 3. pp. 119–123.

Experiences with atebrin in Tanganyika Territory in prophylaxis and treatment of malaria.

The observations were made during the fever season, which corresponds with the rainy season, and during this period fresh infections are always occurring. The prophylaxis was undertaken in natives amongst whom adequate control observations could be carried out. Sixteen adults and 14 children were given atebrin as a prophylactic. The author's scheme was to give one tablet, 0·1 gram., atebrin on Monday, Wednesday, Thursday and Saturday for six weeks as this is the maximum period for the rainy season. Children received smaller doses, 0·05 gram, half a tablet 1–6 times weekly according to age. Without exception the adults and children remained free from fever and fit for work, whilst many of the controls had fresh infections with parasites in the blood. After cessation of the atebrin the controlled observations were continued for 4 weeks longer, and it was found that of those who had taken atebrin only one person, a 12-year old boy, developed fever with rings of malignant tertian in his blood, all the rest remained well. Following this satisfactory result, the author advised all Europeans, who lived in malarial districts, to adopt this prophylaxis and reports received are satisfactory.

For the treatment of severe malaria he has found the new preparation, atebrin musonate, very useful. He prefers the dry powder to the prepared solution. Each ampoule contains 0·1 gram, and this is dissolved in 3 cc. distilled water and given intramuscularly ; in more urgent cases intravenously, injected very slowly. Later he gave 0·2 gram in 5 to 6 cc. water. For small children the dose was 0·03 to 0·05 gram, intramuscularly. For children of 10 and over, 0·06 to 0·1 gram. per dose. It was well tolerated. He considers that the injections are valuable in severe cases of malaria with loss of consciousness and intestinal disturbances, which interfere with oral administration. He follows up the injections with oral administration of atebrin and plasmoquine simplex. *E. D. W. Greig.*

VOORHOEVE (H. C.). Een nieuwe vorm van chininetoediening bij malaria. [**A New Form of Quinine Administration in Malaria.**]— *Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. June 9. Vol. 76. No. 23. pp. 1441–1449. [10 refs.] English summary.

Six years ago TABOLOFF, in order to counteract the tendency of quinine to bring about a leucopenia, suggested the quinine being given intramuscularly with glycerol, iodine and adrenalin. The author first compared the results, as regards the white cell counts, of giving the new mixture to 10 persons, and of giving injections of quinine to 10, and using another 10 as controls. He did not find the first presented any increase in leucocytes. He then carried out a larger series of tests : to 37 persons with tertian malaria were given quinine tablets, to 70 quinine bihydrochloride in solution, to 120 quinine in ampoules, 12 were treated with aristoquine, 52 with quinoplasmine and 57 with the iodine quinine. In a table the results are given, divided into 3 groups : (1) those in whom the temperature fell by crisis ; (2) those with lytic fall, and (3) those with an irregular temperature curve. In 34·4 per cent. (11 persons) of the quinine tablet group, in 28·6 per cent. of those having the solution and in 40·4 per cent. of the quinoplasmine group, the temperature fell by crisis ; in 56·2 per cent. of the quinine mixture group. Not only was this better result observed on the fever, but also in disappearance of plasmodia with this drug. Two cases with splenic

enlargement not reduced by other methods showed considerable reduction with the iodine quinine mixture. The mode of preparation of this mixture is as follows :—

8 gm. bihydrochloride of quinine are dissolved by aid of heat in 5 cc. distilled water ; next, 0·2 gm. iodine is dissolved in 22 cc. glycerin, and the two solutions mixed, filtered while warm and sterilized by heating in a water-bath for 15 minutes and 1 cc. of 1/1,000 solution of adrenalin hydrochloride added. The author says that he has not confirmed the statement that after 12 hours a precipitate settles down and that it is advisable therefore to heat the mixture to the body temperature before injecting it.

H. H. S.

KUBO (M.). **On the Alleviation of the Toxic Symptoms of Quinine.** —*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Jan. Vol. 35. No. 1 (370). [In Japanese pp. 196–204. English summary p. 205.]

This is an account of experimental work carried out on white mice to show the effect of stimulation of the reticulo-endothelial system on combating the ill-effects of quinine. The author found that quinine given in a dose of 0·03 cc. of a 0·7 per cent. solution per gm. bodyweight caused death in a little over 5 days, average 5·3. If at the same time the same dose of 0·5 per cent. egg-albumen was injected, death did not take place till 20·7 days ; with the same dose of double strength albumen (1·0 per cent.) death occurred a little earlier, average 20·0 days. Stimulation by exposure to ultra-violet rays, though prolonging the interval, was not so effectual as the egg-albumen. Thus, after exposure to the rays for 6 days, the quinine was injected, and the animal exposed to the rays at a distance of 50 cm. for 20 minutes twice daily ; death occurred after an average of 15 days. *H. H. S.*

SANDERS (J. P.). **Treatment of Malaria with a Short Course of Quinidine.**—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 651–660.

Plantation negroes treated successfully with 4 or 5 day courses of quinidine consisting of 40 to 70 grains in all.

From 1930 to 1933, the author employed quinidine or quinine in 10 grain doses once a day for 4 days. Quinine stopped the fever in about 4 days, quinidine in about 2. Malaria became more prevalent and severe after a flood in 1933 and from then onwards the treatment was altered to a five-day course of quinidine : 20 grains on each of the first 2 days and 10 grains on each of the other three. A total of 1,047 cases, in 864 individuals, was treated during the 5 years 1930 to 1934 by the short course of quinidine ; 420 benign tertian, 243 subtertian, 384 no parasites found. " The patient was practically always well in less than a week and back at work, a result most satisfying to patient, physician and plantation owner." The quinidine was purchased in 5 grain capsules, and the average cost per patient was apparently about 25 cents per annum. This work was done near Shreveport, Louisiana, and most of the patients were plantation negroes. [Presumably they were a relatively immune population and responded readily to treatment.] *W. F.*

Barbosa (Amando). La quinina y la asociación quinina-plasmoquina en la prevención de las recidivas de terciana benigna. (Estudio comparativo.)—Reprinted from *Africa Médica*. 1936. No. 8. 15 pp. With 2 graphs.

Sonnenschein (C.). Schädigung durch Plasmochin-Ueberdosierung. [**Damage from Overdosing with Plasmoquine.**]—*Arch. f. Schiffs- u. Trop. Hyg.* 1936. Apr. Vol. 40. No. 4. pp. 165–166.

A case is described which presented the typical picture of plasmoquine poisoning of average severity and this was ascribed to relative overdosing and to the simultaneous administration of plasmoquine and atebrin. The patient weighed only 48 kgm. and had suffered from several malarial relapses, flagellate colitis and anaemia. In 5 days she had taken, as well as atebrin, 15 tablets of plasmoquine each 0·01 gm., and in addition 0·06 gm. plasmoquine was given by injection. In all 0·21 gm. plasmoquine within four and a half days. The author warns against the simultaneous administration of plasmoquine and atebrin.

E. D. W. Greig.

Decourt (P.). Etudes sur la toxicité de la praequine (plasmochine) et de la rhodoquine (710). (Deuxième note.) [**The Toxicity of Praequine (Plasmoquine) and Rhodoquine (710).**]—*Bull. Soc. Path. Exot.* 1936. Mar. 11. Vol. 29. No. 3. pp. 328–336.

The two drugs given together exert a combined therapeutic action, but not a combined toxic action.

These drugs are not equally toxic for all laboratory animals, but generally speaking praequine is twice as toxic for them as rhodoquine. In man they are of equal toxicity. The sign of intolerance of praequine is cyanosis with the formation of methaemoglobin ; it attacks the blood corpuscles and the myocardium, both of which are of mesodermic origin. Rhodoquine, in big doses, does not produce cyanosis ; it attacks the nerve cells which are of ectodermic origin, and it causes vertigo and palsies. It is often convenient to give a gametocidal drug at the same time as atebrin or quinine is given, though it is safer to give it as a separate course of treatment. For example, 0·3 gram atebrin with 0·03 gram plasmoquine daily for 5 days was followed by toxic symptoms in several cases. It occurred to the author that as praequine and rhodoquine had entirely different toxic actions, it was probable that if they were given together, they would in no way help one another to poison the patient. He carried out many experiments on animals which confirmed his hypothesis that when two drugs exert their toxic action on systems of different embryological origin, they do not associate their toxicity when they are given together. For example, when a dose of x grams of praequine was given to mice, 55 per cent. died, and when y grams of rhodoquine were given 40 per cent. died. When, however, x grams of praequine and y grams of rhodoquine were given together, not 55+40 per cent., but only 55 per cent. of the mice died. He next tried the mixture on man and found that it acted in the same way. The gametocidal, therapeutic action was the sum of that of each of the drugs, but the toxic action was not. He recommends that these two drugs should be given together in equal quantities for 3 days and that the daily dose of the mixture should never exceed 0·03 gram. This treatment has been extensively employed for the last 2 years without causing any toxic symptoms.

W. F.

Hoops (A. L.). **The Advantages of Atebrin in the Treatment of Malaria amongst Controlled Labour Forces in Malaya.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Nov. 25. Vol. 29. No. 3. pp. 249–259. [38 refs.]

" Atebrin is the best drug available for the controlled treatment of all types of malaria in Malaya."

The labour forces in question number some 20,000. The atebrin treatment consisted of 0·3 gram daily for a period of 5 days. If the temperature was above 99°F. on the third or fourth days, the treatment was continued for one, or for two, days longer. In subtertian cases and in some relapsing cases of benign tertian, the atebrin was followed by a five-day course of plasmoquine, 0·01 gram three times a day. This was the treatment for adults and for children over 10. Smaller doses were given to younger children, but those under 6 were not given plasmoquine without special orders. The quinine treatment which was formerly employed consisted of 30 grains a day for the first week or ten days, and 10 grains a day for 3 weeks. Atebrin treatment actually costs less, and there is a still greater saving effected by the low relapse rate, lessened absence from work, and greater efficiency. Atebrin is not a substitute for antimalarial measures such as drainage and oiling, but it is a great adjunct to them.

Atebrin has been in use on the Malacca Estates since the middle of 1932, and since then the numbers of deaths and the numbers of patients admitted to hospital have been less than in any year since they were first recorded in 1925. This improvement the author attributes partly, but not entirely, to the use of atebrin. No case of blackwater fever has occurred since the middle of 1932. The relapse rate has been very low : in 600 cases, observed for at least 8 months after treatment, it was about 15 per cent. in benign tertian, and 7 per cent. in subtertian ; " it is to be borne in mind that some of the further attacks of malaria must have been new infections though all are counted as relapses." There were very few toxic symptoms. In 1,207 cases there was only one case of cerebral excitement ; this was a male Tamil in whom the condition developed on the 4th day of treatment and passed off in 3 days. Severe headache occurred in a few patients. Violent vomiting was rarer than with quinine. Severe colic occurred in 9 patients, 7 of whom were taking plasmoquine. The author states that he is not in agreement with those workers who prefer to allow the patient to pass through several attacks of malaria, controlled by small doses of quinine, with the object of producing immunity. He argues that this must produce a number of reservoirs for the spread of infection and he writes, " we aim at preventing the reinfection of the cured sufferer from malaria and we therefore do not take the risk to himself and others of trying to produce a possible immunity." With this object he has employed atebrin instead of quinine since the middle of 1932, on all the estates of the Malacca Agricultural Medical Board. (See Hoops, this *Bulletin*, 1933, Vol. 30, pp. 476 and 843 ; 1934, Vol. 31, pp. 678 and 695.) *W. F.*

Seckinger (Daniel L.). **Atabrine and Plasmochin in the Treatment and Control of Malaria.**—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 631–649. With 2 figs. [21 refs.]

In rural malaria where drainage is impracticable, atebrin and plasmoquine are of great value in a country where there is a definite malaria season.

This study was made in an area of Calhoun County, Georgia, where drainage would be very difficult because of the numerous lime-sinks. The area is entirely rural ; it is 54 miles square with a population of 1,325, most of whom are negroes. The parasite index of the school children in the autumn of 1932 was 80 per cent. Two adjacent areas were selected, one for treatment and one as a control. The treatment was as follows : plasmoquine 0·01 gram, three times a week was given to everyone in the treated area, and, whenever anyone had malaria, he and all his household received a five-day course of 0·3 gram atebrin daily. This treatment was carried out in the malaria season, which lasts from May until the end of October, during the years 1933 and 1934. The result was a very material reduction in infection : at the beginning of treatment in 1933, 24·7 per cent. were infected ; at the height of the malaria season in October, only 10·9 per cent. The corresponding figures in the control area were 29·3 in May and 60·3 in October. The crescent rate in October was 21 per cent. in the treated area and 36 per cent. in the untreated. The results in 1934 were equally good, but were complicated by treatment of the control group during October. [There is also the complication of a misprint in the tables.] The percentage of those originally negative who subsequently became positive was 27·8 in the treated area as compared with 69·0 in the control area. Komp and Clark who attempted the control of malaria with drugs in isolated villages in Panama did not meet with success. [This *Bulletin*, 1935, Vol. 32, p. 784.] The author discusses the reasons for the different results. (1) In Panama, mosquitoes and malaria are present throughout the year, but in Georgia there is a definite malaria season followed by a period of 6 months during which there is little or no transmission. (2) The Panama experiment was made in villages, where an infected mosquito may easily infect a large number of people, but the author's investigations were made in a very sparsely populated rural area.

W. F.

Hay (D. C.), Spaar (A. E.) & Ludovici (H. L.). **Atebrin Treatment in Malaria.**—*Indian Med. Gaz.* 1935. Dec. Vol. 70. No. 12. pp. 678–679.

No abscess resulted in 3,500 cases treated with injections. Mental disturbance occurred in about 5 cases per 1,000.

The authors have treated 3,500 patients in their private practice with two injections of either atebrin dihydrochloride or atebrin musonate. In each case, the injections were followed by a six-day course of two 0·1 gram tablets of atebrin daily by the mouth. Each of the two injections consisted of 0·15 gram of the dihydrochloride, or its equivalent in musonate, bringing the total quantity up to 1·5 grams of atebrin for an average adult. The therapeutic results were excellent. There was not a single case of collapse after injection, nor any death attributable to the drug. No abscesses occurred in the whole series, and pain at the site of injection was negligible. Cases of mental excitability occurred in about 5 cases per thousand, and occasionally patients complained of headache, restlessness and insomnia. Toxic symptoms, on the whole, were rare : one patient confessed, after an injection of the dihydrochloride, that he had already swallowed 10 tablets on that day, but no ill-effects followed, and the man was back at work within 24 hours. Mental symptoms when they occurred were readily controlled by sedatives.

W. F.

i. UDALAGAMA (Lyn). **Mental Derangement in Malaria Cases treated by Atebrin-Musonate Injections.**—*Indian Med. Gaz.* 1935. Dec. Vol. 70. No. 12. pp. 679–683.

ii. INDIAN MEDICAL GAZETTE. 1935. Dec. Vol. 70. No. 12. pp. 687–688.—**Malaria, Atebrin and Mental Disturbances.**

i. Details of 7 cases.

The standard treatment with atebrin musonate was two injections, each equivalent to 0·3 gram of atebrin, with an interval of 24 hours between the injections. [This is double the dose given by HAY and his colleagues, see above.] Mental symptoms appeared in 7 out of 644 cases treated as out-patients at the Narammala Field Centre, Ceylon. All the patients were examined as to fitness for treatment, and they were given food before and after the administration of the injection. The following is a short abstract of the details of the 7 cases given by the author.

Onset.	Duration	Symptoms
1. 2 hours after 2nd injection ...	17 hours	Abusive, restless and violent. Memory a blank for this period
2. 3½ hours after 2nd injection ...	36 hours	Severe headache, talking incoherently, restless
3. 1 hour after 2nd injection ...	?17 days	Dazed and indifferent to surroundings. Transient symptoms after 1st dose
4. 2½ days after 2nd injection ...	42 days	Gradual onset; made mistakes in writing out the charms by which he made his living. Later became violent, threatened to kill wife and was removed by police. Memory a blank for period of mental disorder
5. 1½ hours after 2nd injection ...	not yet recovered	Irritable, sleepless and melancholic
6. ? 12 hours after 2nd injection	died	Dazed
7. 1½ hours after 2nd injection ...	8 days	Violent and abusive

ii. The dangers of atebrin have been exaggerated.

The writer of this leading article considers that the effect of atebrin in producing mental disturbance has been exaggerated; "these ill effects have been attributed to atebrin *per se*, and a false impression has been created. . . . However, the evidence that we now have before us does seem to indicate that there is some aetiological connection between these mental disturbances and the administration of atebrin *in a malarial subject.*" He points out that the symptoms in cases 6 and 7 of Dr. Udalagama's series were probably not due to atebrin, and that therefore the incidence of mental symptoms was about one in every hundred cases treated. Dr. HAY and his colleagues (see above) used doses only half as large, they saw only half as many cases of mental

disturbance, and such as occurred were mild, of short duration and easily controlled by sedatives. *W. F.*

Foy (Henry), Kondi (Athena) & Peristeris (Michael). **Studies on Atebrin. A Controlled Field Experiment to test the Relapse Value of Atebrin.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. June 30. Vol. 30. No. 1. pp. 109–114.

The object of the observations described in this paper was to determine the malaria parasitic relapse rate after treatment with atebrin. The inquiry was carried out in the village of Samsus, about 38 miles inland from the western coast of Epirus (Greece). In January 1933, when the work was begun, the spleen rate of the village was 92 per cent. and the parasite rate 39 per cent. (*P. vivax* 68 per cent., *P. falciparum* 20 per cent., *P. malariae* 4 per cent., mixed 7 per cent.) In the previous August the parasite rate had been 58 per cent. The season of active malaria transmission in Greece is from June to October; the observations were thus carried out at a period when new infections were at their lowest or non-existent.

Two hundred villagers were selected at random, avoiding, however, children under five years of age. The blood of each was examined on three successive days, on the last of which treatment was begun. For treatment these villagers were divided into four groups. To each member of the first group atebrin was given; 0·2 gram a day for five days to children, 0·3 gram a day for five days to adults.

The members of the second group received quinine and plasmoquine each day for five days as follows:—

ages 5 to 10, 0·8 gm. quinine + 0·01 gm. plasmoquine
,, 10 to 15, 1·5 ,, + 0·01 ,,
,, above 15, 2·0 ,, + 0·02 ,,

The members of the third group received quinine alone for five days as follows:—

ages 5–10, 0·8 gm. quinine; 11–15, 1·5 gm.; above 15, 2·0 gm.

The fourth group was the control group to each member of which bicarbonate of soda was given.

The blood of all persons under observation was re-examined on three occasions during the first week of May and the percentage of those harbouring demonstrable parasites is the relapse rate of the authors. In the atebrin group this relapse rate was 12 per cent.; in the quinine and plasmoquine group, 17·5 per cent.; in the quinine group, 27 per cent.; in the control group the May infection rate was 36 per cent.

[In estimating the parasite relapse rate no account is taken of the infection rates in the various groups at the beginning of the observations. In the atebrin group the infection rate fell from 47 to 12 per cent.; in the quinine and plasmoquine group from 32·5 to 17·5 per cent.; in the quinine group from 33·3 to 27 per cent., and in the control group from 42 to 36 per cent.] *Norman White.*

Carman (J. A.) & Cormack (R. P.). **A Controlled Experiment in the Treatment of Malaria and Atebrin-Musonate by Injection.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Jan. 25. Vol. 29. No. 4. pp. 381–396. With 1 chart.

The results of 3 injections were similar to those of a five-day course of oral atebrin. Symptoms were relieved as readily as by quinine injections and convalescence was shorter.

Thirty-three cases of malignant tertian were treated with atebrin musonate injections and 33 were treated with quinine and plasmoquine. The temperature came down, the asexual parasites disappeared and the short duration of the treatment was a great advantage. There were no toxic symptoms. The authors are of the opinion that the number of relapses was much less than it would have been after quinine. A drawback was the expense : 15 tablets of atebrin costs two shillings, one ounce of quinine costs the same, but one ampoule of atebrin costs half-a-crown. The authors recommend the intramuscular injection of one 0·375 gram ampoule daily for 3 days. The high cost makes it unsuitable for native hospitals, " but the slight inconvenience involved and lack of all unpleasant toxic symptoms make it a strong rival to quinine and oral atebrin for patients able to bear the expense. *W. F.*

Brown (A. Forbes). **Initial Impressions of Atebrin-Plasmoquin in the Treatment of Malaria in Uganda.**—*Jl. Trop. Med. & Hyg.* 1935. Dec. 16. Vol. 38. No. 24. pp. 301–304. With 10 charts.

Atebrin is a better remedy than quinine.

The author's impression after treating 200 cases with atebrin, and plasmoquine, is that further experience will probably bring him to the conclusion that quinine should be discarded in favour of " this shorter, less unpleasant, and, to my mind, more efficacious remedy." The treatment given was : atebrin 0·1 gram and plasmoquine 0·01 gram three times a day, for 5 days. No toxic symptoms were noted. The author states that the retail price of atebrin is 4 shillings for the 15 tablets necessary for a 5-day course—" admittedly expensive, but a course of retail quinine, say of 30 grains daily for 1 week, would be just as expensive and much more unpleasant." [Probably he does not mean to imply that quinine costs more than 8 shillings an ounce in Uganda, but that recovery is so much quicker with atebrin treatment.]

W. F.

Manson (D.). **Atebrin-Plasmochin in the Treatment of Malaria.**—*Indian Med. Gaz.* 1936. Mar. Vol. 71. No. 3. pp. 127–132.

Toxic symptoms occurred in several cases treated with 0·3 gram of atebrin and 0·015 gram of plasmoquine daily for 5 days. In every case there was some abnormality of the gastric juice, either too much or too little hydrochloric acid.

These experiments were carried out in the central hospital of a group of tea gardens in Assam. The patients remained in hospital for at least a week and they were seen once a week afterwards for a period of 6 months. Twenty-one of the patients were treated with atebrin 0·1 gram t.d.s. and 50 were treated with the same dose of atebrin, together with plasmoquine, either 0·0033 or 0·005 gram with each dose, the small difference in quantity made no apparent difference. Treatment in both groups lasted five days. The fever and the parasites disappeared rather more quickly in the plasmoquine group, but the numbers are small. Six cases are recorded in which toxic symptoms occurred in the plasmoquine group. In two cases there was hyperchlorhydria, in three cases there was complete achlorhydria, in one there was cholecystitis. The author concludes that " there seems to be a definite connexion between achlorhydria, the biliary system, and the

production of toxic symptoms after the exhibition of atebrin and plasmochin." Two of the patients who suffered from toxic symptoms were subsequently given the same drugs in keratin coated dragées without ill effects. The percentage of relapses in these patients, treated either with atebrin alone or with atebrin plus plasmoquine, was about 11 per cent. in 6 months, as compared with 40 per cent. after quinine treatment. *W. F.*

Chopra (R. N.), Gupta (J. C.) & Sen (B.). **A Comparative Study of the Action of Atebrin and Atebrin-Plasmochin Combination on Indian Strains of Malaria.**—*Indian Med. Gaz.* 1936. June. Vol. 71. No. 6. pp. 309–313.

This report from the Department of Pharmacology of the Calcutta School of Tropical Medicine gives the results of treatment of fifty-four cases of malaria in the Carmichael Hospital, with atebrin-plasmoquine and compares these results with those obtained by the treatment of a previous series of cases with atebrin alone. The preparation used was Bayer-Meister Lucius dragées containing 0·1 gm. of atebrin and 0·0033 gm. of plasmoquine. One dragée given three times a day for five consecutive days was the "usual dose for an adult." Twenty cases were infected with *P. vivax*, 19 with *P. falciparum*, 4 with *P. malariae* and 7 were mixed infections. The age and sex of the patients are not given. All patients were kept under observation for at least a fortnight after treatment, daily blood examinations being carried out.

The authors conclude that, in so far as the disappearance of parasites from the blood is concerned, the combination of the two drugs is no more effective than atebrin alone in benign tertian and quartan infections. Practically all *P. vivax* had disappeared on the fifth day. In malignant tertian infections, however, the combination is more effective. On the sixth day 86·5 per cent. of the cases so treated showed no parasites, whereas in only 55·5 per cent. of cases treated with atebrin alone were no parasites found. The relapse rate in all forms of infection is definitely lower if treated with the two drugs combined. Figures on which this conclusion is based are not given. There appeared to be no relationship between the number of parasites in the peripheral blood and the time taken for their disappearance under treatment.

Norman White.

Govindaswamy (M. V.). **Atebrin Poisoning.** [Correspondence.]—*Lancet.* 1936. Jan. 4. pp. 56–57.

A man aged 32 was admitted to the Mysore Government Mental Hospital with symptoms resembling delirium tremens. He was a total abstainer. He shouted that he saw snakes and fantastic animals crawling on the floor, and he reacted to these hallucinations with so much fear and violence that it was necessary to restrain him. The pupils were dilated; nystagmus was present; speech was slow and hesitating; there were fine tremors of the tongue and hands. The pulse was rapid and he was deeply jaundiced. His temperature was normal; no malaria parasites were found. His mental symptoms cleared up in 3 days, and the jaundice in 7 days. During the 8 days before admission he had been given two atebrin pills daily, and 3 injections of atebrin musonate. *W. F.*

KEHAR (N. D.). **Observations on the Absorption and Excretion of Atebrin.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 393–404. With 4 graphs. [26 refs.]

Oral atebrin is rapidly absorbed and can be detected in the urine 15 to 30 minutes after a single dose of 0·3 gram.

Volunteers were given three doses of atebrin by the mouth, with an interval of one or three hours between the doses, and their urine was examined by the method of WATS and GHOSH (this *Bulletin*, 1935, Vol. 32, p. 749). Monkeys were given injections of atebrin dihydrochloride and their urine was examined in the same way. When a single 0·3 gram dose was given by the mouth, atebrin appeared in the urine within 15 to 30 minutes ; when it was given in 0·1 gram doses it took about 60 to 90 minutes. The greatest concentration in the urine occurred during the first 24 hours after a single dose of 0·3 gram, but, when the same amount was divided into 3 doses with 3 hours between them, the greatest concentration occurred on the second day. Qualitatively the presence of atebrin could be detected as long as 55 to 69 days. The greater the amount of the urine, the quicker the rate of excretion. Because of the rapid absorption of atebrin given by the mouth, there can be little advantage in giving it in any other way. In severe cases it may be advisable to give 0·3 gram in one dose on the first day of treatment. From 49 to 69 per cent. of the dose of atebrin was excreted in the urine during 16 to 28 days after its administration. The author questions the accuracy of HECHT's theory which is to the effect that the atebrin is taken up by the duodenum, passed to the liver, and excreted with the bile back into the duodenum. *W. F.*

KEHAR (N. D.). **The Influence of Food in the Stomach on the Absorption and Excretion of Atebrin.**—*Records of the Malaria Survey of India.* 1935. Dec. Vol. 5. No. 4. pp. 405–411. With 1 fig.

A single dose of 0·3 gram of atebrin was given to volunteers (*a*) on an empty stomach, or more than 2½ hours after a meal ; (*b*) less than 2 hours after a meal. A corresponding dose of atebrin musonate was given in the same way. It was found that when the drug was taken fasting, it appeared sooner in the urine, and the quantity excreted during the first 24 hours was greater than when it was taken on a full stomach. Atebrin and atebrin musonate given by the mouth appeared in the urine at the same rate, but the total excreted during the first 3 days was greater in the case of atebrin musonate. *W. F.*

SIMEONS (A. T. W.). **Mass Treatment with Injectable Atebrin.**—*Indian Med. Gaz.* 1936. Mar. Vol. 71. No. 3. pp. 132–137. With 1 chart.

Good results of mass treatment with injections in (*a*) hospital staff, (*b*) isolated village, (*c*) population of 5,650 in a mill area. Dosage scheme. Two deaths followed plasmoquine given after atebrin musonate. Deterioration of solution on keeping. One per cent. of abscesses after inoculation. Ascribed to sepsis.

The staff of Kurunegalle Hospital, Ceylon, numbering 65 persons, was inoculated with 0·3 gram of injectable atebrin (0·375 gram musonate) dissolved in 9 cc. of water ; the inoculation was repeated on the following day. Before treatment, 36 had parasites in their blood. The patients went on with their duties ; the injections were painless,

though in some cases there was subsequent tenderness at the site of inoculation. Two days later, the inoculated persons were all free from parasites. There were no relapses or new infections of the staff during the next 5 weeks, but in the following week there were six.

All the 250 inhabitants of an isolated village in the Kurunegalle district were given two inoculations. Before the inoculations, parasites were present in 40 per cent. A week later, 4·5 were positive, and, during the next 6 weeks, only 7·6 per cent. complained of fever.

At the Godak Mills in the Mahratta country of India 5,650 persons were treated. Healthy adult males were given 9 cc. of a solution containing 0·3 gram of atebrin in 9 cc. of distilled water. Children were given the following doses of the same solution :—

Up to 6 months	0·5 cc.	6 to 10 years	4 cc.
½ to 2 years	1·0 cc.	10 to 12 ,, ...	5 cc.
2 to 4 ,, ...	2·0 cc.	12 to 15 ,, ...	6 cc.
4 to 6 ,, ...	3·0 cc.	15 to 18 ,, ...	7 cc.

Each person was given a second injection on the following day and also 3 tablets of 0·02 gram of plasmoquine with instructions to take one a day. In 4 cases haemoglobinuria occurred after the third plasmoquine tablet had been taken, and two of the four patients died. Abscesses occurred at the site of inoculation in 49 patients ; this is attributed to sepsis. No toxic symptoms attributable to atebrin were seen beyond a few cases of giddiness and fainting. The solution for the day was made up in the morning, and it was noticed that the cases of giddiness occurred in the afternoon, several hours after the solution had been made. If patients were inoculated with a solution which had been kept overnight, there were still more cases. Subsequently, the solution was prepared in small quantities for immediate use, and no more cases occurred. The result of the " blanket treatment " of the mill-hands appears to have been excellent, during a period of 7 months there were only 55 relapses. *W. F.*

Kariadi. Enkele ervaringen met chinine en atebrin bij de behandeling van chronische malaria in verband met het optreden van zwartwaterkoorts te Manokwari (Julianaziekenhuis).—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Apr. 7. Vol. 76. No. 14. pp. 860–879. With 14 charts. [13 refs.]

Ziemann (Hans). Zur modernen Therapie und Prophylaxe der Malaria (speziell mit Atebrin und Plasmochin).—*Med. Klin.* 1936. May 29. Vol. 32. No. 22 (1641). p. 745.

Barbosa (Amando). Un ensayo de profilaxis antipalúdica con atebrina y plasmoquina.—Reprinted from *Gac. Méd. Española.* 1936. No. 114. pp. 3–7.

Decourt (Philippe), Villain (Georges), Marini (Charles) & Dupoux (Robert). Expériences de prophylaxie collective du paludisme par les produits synthétiques effectuées en Tunisie au cours de l'année 1934. [**Prophylaxis of Malaria by Synthetic Drugs.**]—*Arch. Inst. Pasteur de Tunis.* 1936. Jan. Vol. 25. No. 1. pp. 154–198. With 1 fig. & 1 map.

In favour of drug prophylaxis.

The authors used the following drugs separately in a prophylactic experiment. Quinacrine (atebrin) 0·4 gram once a week ; Praequine

(like plasmoquine) 0·03 gram once a week ; Rhodoquine in the same doses ; Quinine 0·4 gram (6 grains) every day. Each group of persons, except the quinine group, was given a preliminary five-days' treatment with quinacrine 0·3 gram daily ; the quinine group received 5 days' preliminary treatment with quinine. The results of 6 weeks prophylactic treatment were good.

With quinacrine, the parasitic index fell from 23 to 0·5 per cent. and the gametocyte index from 21 to 5. The results in the quinine group were almost the same, but its daily administration gave rise to considerable difficulties. The results with praequine and rhodoquine were almost the same.

Next, some 750 persons were given prophylactic treatment once a week with quinacrine and praequine together. There were no accidents. The result in adults was a reduction of the parasitic index from 72 to 42 per cent., while in the control group the figures were 85 and 80·5 per cent. *W. F.*

Ragiot (Ch.). Paludisme au cours de la fièvre typhoide. Action de la quinacrine. [**Malaria in Typhoid Fever. Its treatment with Quinacrine.**]—*Rev. Méd. et Hyg.-Trop.* 1935. Nov.–Dec. Vol. 27. No. 6. pp. 315–321.

Some authorities consider that quinine should not be given to patients suffering from typhoid fever, because it might have a bad effect upon a heart already damaged by the disease, and upon a nervous system debilited by fever. The author gives details of 9 cases of typhoid fever complicated by malaria, in which quinacrine (French atebrin) was given without any ill effects, and he recommends this drug for the treatment of malaria occurring during the course of typhoid fever. *W. F.*

Field (J. W.) & Niven (J. C.). **A Clinical Comparison of Atebrin-Musonate with Quinine Bihydrochloride. (A Preliminary Report based on the Treatment of 286 Cases of Acute Malaria.)**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Apr. 8. Vol. 29. No. 6. pp. 647–658. With 7 figs.

A method for detecting atebrin in dilute solution is given. Dosage of atebrin discussed. Two cases of fits following atebrin. Intramuscular route preferred to intravenous. Atebrin musonate acts a little more quickly than quinine.

A series of cases was treated with atebrin musonate (dimethane sulphonate of atebrin) administered either by intramuscular or intravenous injection. For intramuscular injection the contents of one ampoule were dissolved in 2·5 cc. of sterile tap-water. Solution was complete in 3 minutes. One ampoule contains 0·375 gram, which is equivalent to 0·3 gram of atebrin, and in this paper the doses are expressed in terms of the content of atebrin. The most satisfactory dose was found to be two injections of 0·3 gram on successive days. Two doses of 0·1 gram were inefficient and the response to a dose of 0·2 gram was slow. It is unnecessary to give the drug intravenously ; traces appear in the urine within ten minutes of an intramuscular inoculation which indicates a rate of absorption quick enough for the treatment of the gravest infection. The manufacturers recommend that the dose for intramuscular injection should be dissolved in 10 cc.

of water, but the authors found that this was rather too bulky, and they used 2·5 cc. without ill effect.

The following technique was employed in examining the urine for atebrin ; 10 cc. of urine is made alkaline with a few drops of saturated potassium carbonate, 0·25 cc. of amyl alcohol is added, and the tube is well shaken. The atebrin is extracted by the amyl alcohol which forms a layer on the surface. By means of ultra-violet light, the typical atebrin fluorescence can be obtained in cases where atebrin is present in very high dilutions. Atebrin appears in the urine a few minutes after injection and then slowly disappears over a period of weeks.

" Throughout the course of the present enquiry 421 intramuscular or intravenous injections of atebrin musonate were given to 176 adults. In no instance were toxic effects of any significance observed which could definitely be attributed to the drug." But, it is stated in a footnote, " we have since observed the occurrence in two subsequent cases of epileptiform fits developing shortly after treatment." [The Sectional Editor has been informed that the atebrin was given intramuscularly.] Intramuscular injections caused remarkably little pain or tenderness. In a few instances there was some induration for a day or two. *Intravenous injections were usually associated with temporary giddiness and faintness, sometimes lasting an hour or more.*

A control series was treated with quinine bihydrochloride administered orally in solution twice a day for 7 days at a dosage calculated according to body weight. In all, 286 cases of acute malaria were treated in alternating sequence with either atebrin or quinine. The result of the comparison is stated by the authors as follows : " There was a tendency for trophozoites to disappear from the peripheral blood and for temperatures to fall to normal somewhat earlier among cases treated with atebrin musonate . . . . It was not possible to obtain precise data regarding the permanency of cure . . . relapses after atebrin musonate treatment are probably fairly common." Judging from the graphs given in this report, there is very little to choose between the two drugs (especially in subtertian) with respect to their action on the parasites and the fever. *W. F.*

Mackay (R.). Notes on the Cinchona Alkaloids in the Treatment of Malaria.—*East African Med. Jl.* 1936. Feb. Vol. 12. No. 11. pp. 336–341.

Marneffe (H.). La moustiquaire en prophylaxie antipaludique. Son application à la protection des collectivités en Indochine.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Nov. Vol. 13. No. 9. pp. 1264–1297. With 9 figs. [15 refs.]

Pareli (Anopheles). " Old " and New Remedies in the Treatment of Malaria."—*Bombay Med. Jl.* 1935. Oct. & Nov. Vol. 4. Nos. 10 & 11. pp. 157–168 ; 199–210. [15 refs.]

MISCELLANEOUS.

Ingersoll (Winifred). **Hemoglobin Values in Normal Adults over a Period of Time.**—*Jl. Lab. & Clin. Med.* 1936. May. Vol. 21. No. 8. pp. 787–789. With 2 figs.

The main outcome of these studies is to show the absurdity of relying on single readings to decide on clinical condition by means of blood examination. The subjects were 30 young adult medical students regarded as being in excellent health and determinations were made weekly or more often from October to January. The author found that the maximum and minimum haemoglobin values varied between 0·4 and 2·7 gm. per 100 cc. Fourteen had a range up to 1·0 gm. and sixteen above this amount. The differences were greater in females, 1·54, as compared with males, 1·1 gm. Nearly half (41 per cent.) showed irregular trends, in general or in weekly values ; some had a fairly constant level. A downward trend during the period was observed in about half, and in 26 per cent. was marked. *H. H. S.*

Schartum-Hansen (Hall). Ergänzung zu " Hämoglobinbestimmung durch Hämatokrit." (Folia Haematologica, Bd. 54, S. 22–26.) Eine leichte Methode zur Umrechnung der Thrombocytenzahl vom Plasma in Blut. [**A Simple Method of estimating the Number of Thrombocytes in Blood.**]—*Folia Haematologica.* 1936. Vol. 54. No. 4. pp. 385–386.

The author has worked out a formula for converting the thrombocyte total as found in the plasma to that present in the blood. It is based on the standard that with 100 per cent. haemoglobin one regards 5 million erythrocytes per cmm. as equivalent to 18·5 per cent. oxygen or 43 volumes per cent., and that 100 per cent. Hb=13·8 gm. per cent. He finds that the Hb percentage divided by 2·6 gives the volume per cent. and from this the formula

$$\frac{\text{Thrombocytes in plasma} \times (100-\text{vol. per cent.})}{100}$$

gives the thrombocyte total in the blood [the *minus* sign in the numerator is erroneously given as a division sign ÷ in the text]. For example, a man 25 years, in apparent health, had Hb 115 per cent., plasma thrombocytes 650,000. The volume per cent. would be 115÷2·6 or 44·2. Then by the formula :—

$\frac{650{,}000 \times 100-44{\cdot}2}{100}=362{,}700$ thrombocytes in the blood. A second example ; a woman of 50 years with lymphocytic leukaemia, had Hb 32 per cent., and plasma thrombocytes 40,000. The volume per cent. is 32÷2·6 or 12·3 and by the formula $\frac{40{,}000 \times (100-12{\cdot}3)}{100}=35{,}080$ thrombocytes in the blood. *H. H. S.*

Matsunobu (M.). Zum Studium der klimatischen Veränderungen der Beschaffenheit des menschlichen Blutes. (Vergleichende Untersuchungen von Erythrozyten, Viscosität, und Erythrozytensenkungsgeschwindigkeit in Sommer und Winter in Taihoku.) [**The Effect of Climatic Changes on Human Blood.**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Apr. Vol. 35. No. 4 (373). [In Japanese pp. 906–912. German summary p. 912.]

Differences in certain constituents and properties of the blood in males and females were examined for in the hot moist climate of summer and the cold damp climate of winter in Taihoku. The erythrocyte total was estimated in 11 healthy men and 23 women in the winter, and in 10 and 23 respectively in summer, 10 of the former and 17 of the latter being the same in both seasons. He found no difference. [Unfortunately the Hb estimations are not mentioned ; they would be interesting in view of the variations found by Winifred Ingersoll, above.] The reticulocytes were found to be a little less, 0·14 per cent. less on an average in summer ; also the viscosity. The red cell sedimentation rate showed greater changes : of 10 men and 18 women tested at both seasons the former showed an increase of 1·73 mm. and the latter 2·45 mm. in summer. The author concludes that in the moist hot summer there is a diminution in the erythrocyto-poietic functions. [The number of examinations carried out during the different seasons is not stated ; if only one in each the results could be of much less value than if the figure given represents the average of several.] *H. H. S.*

Giglioli (George). **Megalocytic Anaemia of East Indians in British Guiana.**—*British Guiana Rep. Surgeon-General for Year 1934.* Appendix II. (B). pp. 94–110. [16 refs.]

The object of this Report is to draw attention to the high incidence of megalocytic anaemia among East Indians of British Guiana, where the disease influences considerably the maternal, foetal and infant morbidity and mortality. Negroes, aborigines and people of mixed races were not affected. Frequently multipara gave a history of similar anaemia during the previous pregnancies which had often terminated with abortion or miscarriage or the delivery of a still-born or sickly infant which did not survive. The ratio of female to male cases was as 5·5 : 1·0, and the ages ranged from 11 months to 44 years. Only 6 cases were seen in children below 12 years. The greatest incidence occurred in adults between the ages of 17 and 30. Of the 38 adult women affected, 35 were expectant mothers or had recently been delivered.

Clinical features.—The onset was generally gradual. Symptoms included lassitude, progressive weakness, palpitation, dyspnoea and vertigo. Soreness of the tongue and mouth, anorexia, dyspepsia and epigastric discomfort after meals were not infrequent. The complexion was muddy with a yellowish tinge, the mucous membranes were pale and the sclerotics subicteric or frankly jaundiced. In 28 out of the 45 adult cases there was fever. Splenomegaly, attributed to malaria, was present in 47 of 50 cases. The stools were bilious, yellow or dark green. Cardiovascular disturbances including dyspnoea, palpitation, vertigo and haemic murmurs were noted. The urine was high coloured and diminished in quantity with transitory albuminuria in 12 out of 51

cases. The nervous system was not involved. Relapses and remissions were a not infrequent feature of the disease.

Haematological findings.—The red cell count varied from 800,000 to 3,700,000 cells per cmm. The haemoglobin percentage ranged from 25 to 40 per cent. (Hellige haemometer). The colour index varied in 7 instances from 1·0 to 1·6, and in 11 from 0·8 to 1·0 ; in 20 it was below 0·8. The lowest figure reported was 0·55. In severe cases it was practically always high. Had the Haldane scale been adopted a larger proportion of cases would have shown a higher colour index, since an 80 per cent. Hellige corresponds to a 100 per cent. Haldane. The reticulocyte count was frequently high and in 34 cases the author points out that the effect of malaria could not be excluded. For the estimation of cell diameters Eve's halometer was used. In 45 patients the average red cell diameter varied from 7·8 to 8·39 microns. The white cell counts generally revealed leucopenia ranging from 3,000 to 5,000 leucocytes per cmm. The serum bilirubin was increased ; 23 out of 31 cases gave a positive Fouchet reaction. The indirect van den Bergh was positive in 39 cases, the readings varying from 2 to 16 units. Only in 2 cases was the reaction negative ; 3 gave a very faint delayed positive reaction.

Treatment.—With a few exceptions, all the patients suffered from malaria, so that a 10 days' course of quinine, gr. 10 twice daily, was given as a routine in both pregnant and non-pregnant cases. Sepsis and intercurrent diseases, such as ankylostomiasis and syphilis, were also treated. Hydrochloric acid was prescribed for dyspepsia. Fresh, raw, or cooked liver or liver extract given by the oral or parenteral route, was utilized. Campolon was injected daily (2 cc.) or larger amounts were given at intervals, *i.e.*, 5 cc. every 4 days. In mild or convalescent cases the interval was increased to 6, 8 or 10 days. Marmite was given in a dosage of 2 drachms by weight twice daily in water, milk or food. Its action was not quite so prompt as the liver extract injections. Marmite was cheaper, but owing to its high salt content required much fluid diluent, and in grave cases with impaired gastric function and vomiting it was not well tolerated. The diet adopted was light and nutritious, and as soon as possible eggs and milk were included. Bulky carbohydrates were avoided. A reticulocyte reaction was noted about the fifth day following marmite and liver extract therapy. As soon as the uterus was emptied, whether by abortion, miscarriage or delivery at full term, recovery followed at a surprisingly rapid rate in the vast majority of pregnant cases. In most patients it took 3 to 4 weeks after delivery for recovery to ensue.

[The author states that this form of megalocytic anaemia, though similar to tropical megalocytic anaemia of India and Africa, differed in that practically all cases gave a positive indirect van den Bergh reaction and in this respect resembled the megalocytic anaemia of pregnancy occurring in temperate climates. Considering, however, that " the effects of malaria could not be excluded in 34 cases of the series," and that " with few exceptions all cases suffered from malaria," this observation loses much of its significance. The problem was also involved by the presence of other intercurrent diseases such as ankylostomiasis (14 per cent.), syphilis (14 per cent.) and sepsis. The incidence of acid secretion in the stomach was not determined nor was it possible for the author, under the circumstances of the investigation, to use more accurate and elaborate methods such as the Price-Jones' curves or volume index in determining the megalocytic nature of the anaemia, or

to examine the marrow obtained by sternal puncture. Despite its inevitable limitations from a haematological viewpoint, the investigation is a valuable contribution and the subject one well worthy of more detailed study.] *N. Hamilton Fairley.*

Napier (L. Everard) & Das Gupta (C. R.). **Haematological Studies in Indians. Part V. Red Blood Cell Measurements. With Note by** K. C. K. E. Raja.—*Indian Jl. Med. Res.* 1936. Apr. Vol. 23. No. 4. pp. 973–992. With 2 figs. [16 refs.]

This article will well repay careful study. The authors discuss without bias the various methods in use for determining red cell measurements—the halometer, the method of Price-Jones, the variations due to the distance of the cells from the centre of the film, variations in different parts of the film ; the packed-cell method of estimating cell volume and a consideration of the " normal " volume in Indians and in " normal " Assam tea-garden coolies [*ante*, p. 75]. They maintain that the halometric method is fraught with possible errors ; so much so as to be of no practical value. The Price-Jones' method is accurate and therefore valuable, but is very laborious. They suggest a means of lessening this, but conclude that it is not altogether practical. The packed-cell method of the authors utilizes 0·2 per cent. potassium oxalate as an anti-coagulant, and as a result of controls with hirudin or heparin they adopt Wintrobe's procedure of multiplying the cell-volume readings by the factor 1·09 and accept his figure of 8·2 per cent. Examination of the cell-volume, total red corpuscles and the haemoglobin in grams per 100 cc. of the blood of 30 city-dwelling male Indians in apparent good health and of 34 Assam tea-garden coolies who had recovered from anaemia has shown that the mean corpuscular volume of the former is higher than British and American standards while the mean concentration of Hb is lower ; among the Assam coolies the cell-volume was low. The authors conclude that the packed-cell method supplies practically all the required information :—

" The fallacies, other than those connected with inaccuracies in the graduation of the tubes, are due to the shrinkage of the cells on addition of the anti-coagulant and to the speed of the centrifuge ; the former can be overcome by using a constant quantity of oxalate and multiplying the reading by a factor, and by using the same centrifuge at the same speed for all one's estimations, both in normals and in anaemic patients, errors due to the latter can be reduced to a minimum. The question of the effect of speed of centrifugalization seems to require further investigation."

H. H. S.

Pai (H. C.). **The Polynuclear Count in Health and Disease and its Significance in China.**—*Chinese Med. Jl.* 1936. Feb. Supp. No. 1. pp. 13–20.

The following as determined by W. E. Cooke may be taken as representing the average Arneth count of healthy subjects in Britain. I 10, II 25, III 47, IV 16, V 2. It varies, of course, but speaking generally a percentage over 40 in I and II together was regarded by him as abnormal. The author studied the condition in apparently normal Chinese in Mukden (Manchuria) and found the average standard to be I 26·7, II 43·7, III 25·4, IV 4·0, V 0·2, *i.e.*, I and II together 70·4. In septic affections the shift to the left was much greater than in the case

of British at home. Thus in acute appendicitis, osteomyelitis, acute tonsillitis I and II made up 97–99 per cent., in scarlet fever and uncomplicated measles 100, uncomplicated whooping cough 91, in the two last with broncho-pneumonia 99 and 97·5 per cent. respectively.

The author has found the I and II percentage and changes in it of value in diagnosis and prognosis ; in the former case particularly where an expected leucocytosis is not present. Thus, he records the case of a man with chills and fever ; Widal negative, blood culture negative, no plasmodia, no physical signs. Leucocytes on two occasions totalled 5,937 and 7,500, with 73–75 per cent. polymorphonuclears. On a third occasion, they totalled 6,600, but an Arneth count gave I and II 99 per cent. Antrum suppuration was found. In prognosis, the value of this percentage is exhibited by two instances. The first a man with peritonitis the result of perforated inflamed appendix. For nearly a week the figure remained 90–96, and then followed a steady shift to the right, 79, 73·5 four days later, and 62 in another three weeks ; the patient recovered. The second was a case of streptococcal septicaemia ; the figures on the first 3 counts at weekly intervals were 99, 98, 89, but after that a return movement to the left took place and 9 days later was 100 and soon afterwards death occurred.

Considering the above findings we may say that the healthy Chinese in Mukden shows a marked shift to the left as compared with the British at home. It would appear to be not a *racial* difference, but rather domiciliary, as the following indicates, where the Chinese in Britain has a lowered figure, returning to the higher " normal " on return to Mukden.

Nationality	Place	Duration of residence	I	II	III	IV	V	I & II
British	Britain	—	10·0	25·0	47·0	16·0	2·0	35·0
,,	Mukden	Over a year ...	32·6	41·2	23·0	3·1	0·1	73·8
Chinese	,,	Over 10 years	33·5	46·0	18·25	2·25	0·0	79·5
,,	Britain	Two months after arrival	12·0	30·0	44·0	12·4	1·6	42·0
,,	Mukden	One month after return	27·5	46·0	24·0	2·5	0·0	73·5

Bannerjee from estimations on Indians in Bengal, Breinl and Priestly on Australian children and New Guinea natives, and Kennedy on natives in Iraq attribute the shift to the left to climatic influence or infections, active or latent. It was found, however, even in subjects in apparent good health, and might be due, at least in part, to environmental factors, high temperature and powerful sunlight. Again, in tropical and subtropical countries the length of life of leucocytes may be shortened, " perishing in middle age," and thus the one- and two-lobed cells would predominate. Why this is so we do not at present know, " but some factor must be at work in Mukden which causes the neutrophil leucocytes to leave the circulating blood much sooner than in Britain, so that relatively few older cells are present." Possibly, as the author suggests :—

" The extreme cold in winter, heat in summer, the strong sun-light, the dusty and dry atmosphere in winter and early spring may in some

way affect the leucocytes and shorten their life, say by rapid passage through the mucous membrane of the upper respiratory tract. In order to determine which of these factors may influence the longevity of the leucocytes, counts of normal individuals at different seasons of the year are being made now."

[Altogether an interesting study and opening up an interesting field of research. See also this *Bulletin, ante*, p. 78.] *H. H. S.*

Tscherkes (L. A.), Litvack (J. I.) & Korovitzky (L. K.). **Sensitivity to Adrenalin in Pellagrins.**—*Acta Med. Scandinavica.* 1936. Vol. 87. No. 5–6. pp. 459–469. [15 refs.]

Attention has been called on several occasions to the similarity existing between the symptoms of pellagra and those of Addison's disease, namely, the disturbances of pigmentation, alimentary dysfunction, anaemia, hypotension, adynamia and asthenia, indicative of dysfunction of the chromaffin system.

The authors have carried out experimental work on man " with a view to establishing in what degree such changes are reflected in the perversion of the reaction of pellagrins to adrenalin." They record here the results in 8 patients. The blood pressure and pulse rate having been ascertained, the patient received, fasting, 100 gm. of sugar dissolved in 300 cc. water and 10–12 minutes later 1 cc. of adrenalin (1 in 1,000) was injected intramuscularly. Thereafter, every 10–15 minutes for an hour the blood pressure, the pulse rate and the state of the pupils were recorded and the sugar content of the urine after 2, 4 and 6 hours. Six of the patients were suffering from acute pellagra and two with a mild form of it. The detailed findings are recorded for each patient, but the results may be summarized as follows : In pronounced cases of the disease there was practically no reaction to the adrenalin, the pulse rate and blood pressure remained almost unchanged, there was no dilatation of the pupils and there was no glycosuria in the time of the experiment, up to 6 hours. In cases of average or slight severity the reaction might be small or absent. Yeast was then given and as the symptoms of pellagra cleared so an increase in the patient's sensitivity to adrenalin was seen.

" All these facts prove that pellagrins suffer from a distinct decrease of the tonus of the sympathetic nervous system, and of the chromaffin system ; they tally well with those clinical symptoms of Addisonism and histopathological disturbances . . . mentioned. . . . The accumulation of further material is requisite for wider generalizations, in which material special attention should be paid to . . . the restoration of sensitivity to adrenalin in proportion to the disappearance of pellagra—a fact which should be borne in mind for the proper interpretation of the pathogenesis of pellagra and for the definition of the effectiveness of therapy." *H. H. S.*

Noosten (H. H.) & Visser (J.). Over de vergiftige eigenschappen van den " Reunghas " (een klinische en experimenteele studie van een blaartrekkende substantie). [**Renghas Poisoning.**]—*Geneesk. Tijdschr. v. Nederl. Indië.* 1936. June. Vol. 76. No. 22. pp. 1346–1404. With 6 figs. & 6 plates. [21 refs.] English summary.

The sub-title of this article is " a clinical and experimental study of a vesicating substance " The researches detailed were undertaken on

account of a patient admitted to the Mission Hospital, Bandung, suffering from extensive dermatitis after contact with the renghas tree—*Gluta renghas* Linn.—which grows near water, and *Semecarpus heterophylla* Bl. often found in cemeteries. The latter was the subject of experiment. Milky juice, obtained by incising the fruit or the bark, produced on contact with the shaven skin of guineapigs or rabbits a local inflammation, sometimes healing in 4 days, at others setting up a dermatitis, persisting, with exudation and necrosis, for weeks. Fresh leaves could be eaten with impunity, and a watery extract of the fruit and other parts, or the vapour from burning the wood were harmless. An extract of the fruit or wood prepared by the Stass-Otto process proved to be very irritant. A drop placed on the shaven skin of guinea-pig, rabbit, or monkey caused hyperaemia, inflammation, exudation and necrosis, lasting for 10 days to several weeks. In the eye it caused severe inflammation and ultimate destruction of the organ. Strange to say, by mouth, intravenously or subcutaneously, no general symptoms resulted. An emulsion obtained by mixing the extract with water was innocuous when applied to the skin, but in ether, in a strength of 1 per cent., it caused inflammation and swelling.

In human beings the extract caused, as in animals, local necrotizing inflammation sometimes extending widely and involving other parts of the body, causing itching and vesication. Possibly, these differences are due to varying susceptibility, or to allergy. Further study is to be taken in hand [see also this *Bulletin*, *ante*, p. 81]. *H. H. S.*

Dierick (J. E. A. M.). **Myiasis intestinalis.**—*Nederl. Tijdschr. v. Geneesk.* 1935. Dec. 21. Vol. 79. No. 51. pp. 5866–5867. With 1 fig. In Dutch. French summary (3 lines).

The case is recorded of a pregnant woman of 26 years vomiting larvae of *Homalomyia canicularis*. The author states that he is unable to conjecture how they came there ; the woman was cleanly, had no sores, and had not eaten any tainted meat, nor for several days any raw vegetables.

H. H. S.

Corradetti (Augusto). Alcune ricerche sull'*Anopheles maculipennis*. [**Notes on** *Anopheles maculipennis* **in Italy.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 2. pp. 106–113. With 1 fig. English summary.

The author presents notes on several points which he has observed in studying *Anopheles maculipennis* in Italy.

The first note describes what appears to be an abnormality in the structure of the shell of the egg of *Anopheles maculipennis labranchiae*. The author failed to find any difference in larval structure or in biology between normal *labranchiae* and those raised from these eggs : the adults were evidently stenogamous (the word " eurygamous " being used apparently as a misprint).

The other notes refer to points of biology. It is found that adults of *labranchiae* bred from the egg are much more willing to feed in the laboratory than adults of other races, and this is irrespective of whether they are given an opportunity of biting man or guineapig, about 80 per cent. feeding on either. Adult *atroparvus* fall into an intermediate group, 40–60 per cent. of them feeding on either of the above hosts. Under similar circumstances less than 10 per cent. of adult *typicus* and

melanoön take blood. It is interesting to see that under the particular conditions of the experiment no evidence of "zoophilism" was obtained.

The author then passes on to statistics of the sex ratio in *labranchiae* bred at different times of the year. His figures appear to indicate that there is no change in sex ratio with season, and that the number of males emerging is generally a little less than the number of females, the percentage of males in the whole experiment (about 4,000 mosquitoes) being 47·81. One would perhaps have expected that the proportion of males would be a little above 50 per cent., assuming that the sexes were in equal proportions in the egg: for it is shown that the males emerge about a day before the females, so that any cause of mortality in the early stages would tend to reduce the proportion of females, because they are at risk for a longer period. *P. A. Buxton.*

Shute (P. G.). **A Study of Laboratory-bred *Anopheles maculipennis* var. *atroparvus*, with Special Reference to Egg-Laying.**—*Ann. Trop. Med. & Parasit.* 1936. Apr. 8. Vol. 30. No. 1. pp. 11–16.

The author presents detailed studies on the biology of the female *Anopheles maculipennis* var. *atroparvus*, giving particular attention to the number of batches of eggs laid and the length of the insect's life.

The mosquitoes have been bred uninterruptedly in the laboratory at 75°F. for about two years. The author's method is to put a number of newly emerged males and females together for 24 hours. The males are then removed and the females fed. As each female shows signs of developing eggs she is isolated until oviposition has occurred. She is then fed and again isolated, it being found that nearly always a single meal of blood is sufficient to produce a batch of eggs. The author has had remarkable success in keeping the insects alive, for about half the females lay 4 batches of eggs and a small percentage of females lay 12 to 17 batches; one of these exceptional females produced in all about 2,500 eggs over a period of 60 to 80 days. In spite of the fact that the females are given only the one opportunity of pairing the fertility of the eggs remains undiminished to the end of the series of ovipositions. The opinion is expressed that though the experiments were carried out in a very uniform way there are differences in the rate of survival in experiments carried out at different times of year, but the figures quoted do not appear to lend much support to this view.

P. A. B.

Stage (H. H.). **Mosquito-Control Activities in the Pacific Northwest under the CWA Program.**—*Jl. Econom. Entom.* 1935. Dec. Vol. 28. No. 6. pp. 1022–1024.

The interest of this account lies in the fact that three different types of anti-mosquito measures were needed to deal with the species concerned. In the thickly matted jungles of willow brush along the Columbia and Willamette Rivers in Multnomah and Columbia Counties, Oregon, and in Skamania and Clark Counties, Washington, flood-water mosquitoes, *Aëdes vexans* and *A. aldrichi*, occur in hordes in summer; their reduction was effected by clearing their breeding grounds of the willow brush, by ditching poorly drained areas and dyking against high water. In the salt-water marsh in Tillamook County, Oregon, *Aëdes dorsalis* breeds in numerous pot-holes between high tides. Under the CWA (Civil Works Administration), elimination was attained by

connecting the pot-holes by ditches to the main channel, whereby the high tides flushed and drained out the breeding places. The third was carried out on the northern end of Bainbridge Island, in Puget Sound. This is a summer resort within easy distance of Seattle. There are many springs and the rugged nature of the district formed depressions where seepage and rain collected and *Aëdes aboriginis* and *A. fitchii* bred abundantly. Pools and seepage were eliminated as far as possible by ditching watercourses to the Sound and where this was impracticable the sites were cleared so that the pools could be oiled without difficulty.

H. H. S.

Escomel (Edmundo) & Chaves Velando (L. A.). Un nuevo Pthyrius parásito de las pestañas del hombre. [**New Species of Louse Parasitic on the Eyelashes of Man.**]—*Crónica Méd.* 1935. Sept. Vol. 52. No. 867. pp. 335–339. With 2 figs.

In 1930 Dr. Chaves Velando observed a case of blepharitis, a child of 2 years, with lice attached to the eyelashes. He regarded them as *Phthirus pubis* transferred to the new site. In 1934 he saw a case in a man of 35 years with obstinate blepharitis, and found many lice and their eggs attached to the hairs of the upper right eyelid, and since then another child of 2 years has been seen by him. In all there were congestion and oedema of the upper lid and a blackish powder on the lower —the excreta of the lice. The authors present in tabular form the comparisons between *Phthirus pubis* and this which they call *P. chavesi*, from which it is seen that the latter is smaller in all dimensions and of a lighter colour.

H. H. S.

REVIEWS AND NOTICES.

GRUNSKE (Friedrich). **Tätigkeit und Ergebnisse der Malaria-Untersuchungsstation in Emden (Ostfriesland) von 1910–1933. Aktenmässige Darstellung einer 24 jährigen Malariabekämpfung in einem deutschen Marschlande.** [Work and Results of the Station for the Investigation of Malaria in Emden (1910–1933).]—*Veroff. aus dem Gebiete des Marine-Sanitätswesens.* 1936. Heft 27. 180 pp. With 6 figs. & 1 folding map. [58 refs.] [7 Rm.]

In this Report a detailed account is given of the activities of the malaria Station in Emden, in East Friesland. The district is flat and marshy, intersected by numerous ditches, dykes and canals, and with many ponds and lakes, mostly at and below sea-level. In the past the area has been liable to frequent flooding, but latterly pumps have been installed to prevent this. The district is situated on the eastern side of the estuary of the river Ems, which separates it from Holland ; on the north it is bounded by the North Sea. The urban area of Emden is about 29 square kilometres, and the population about 30,000, much of the latter being contained in the suburbs of Transvaal and Port Arthur. The extent of the rural area, in which the malaria station works, is about 340 square kilometres, with a population of about 25,000.

Malaria has been endemic in East Friesland, and especially in the Emden district, for centuries. In the past, there have been many widespread epidemics, some of which were very severe. From the year 1880 onward, a decided improvement occurred in the prevalence of malaria ; this took place coincidentally with the partial drainage of the swampy surroundings. In 1908 there were again many cases ; it became necessary to adopt systematic measures to cope with the disease, and the malaria station was opened in March 1910. Since that date there have been several years in which malaria was again very prevalent ; the worst period was from 1917 to 1920. After that, the number of cases fluctuated year by year ; the highest number occurred in 1926, after which there was a gradual fall, reaching a minimum in 1929 and 1932, but there were rises in 1930, 1931 and especially in 1933.

The work of the malaria station consists in the methodical search for cases of the disease, accurate diagnosis by blood-examination, lectures and publication of explanatory and educational pamphlets, and other forms of propaganda. At first the station also undertook the treatment of malaria cases with quinine, and the patients were visited frequently by some of the staff, or by nurses, to make sure that the treatment was being carried out properly. As far as possible, patients were encouraged to seek treatment from the local doctors, though none was refused treatment by the malaria station, and the treatment was free. The doctors were asked to notify to the station all cases of malaria that they saw in their practice, and every attempt was made to obtain their co-operation. Unfortunately the work of the station was not welcomed by many of these practitioners, who were not at all diligent in reporting cases. The chief reason for this aloofness seems to have been resentment of the fact that the station undertook free treatment of persons in whose blood malaria parasites had been found ; but even when the station discontinued this practice, in 1928, and confined its activities to diagnosis, mosquito control, and other general anti-malarial measures, the doctors maintained an attitude of some reserve, which, however, has lessened of late years.

There was also, for a long time, a certain amount of apathy, and even opposition, to the acceptance of treatment on the part of the inhabitants, and this was not entirely confined to the less educated. Many of the people were in the habit of carrying out their own treatment with quinine, which they took in sufficient quantities to stop, at least temporarily, the attacks of fever ; but the treatment was not at all systematic, nor thorough enough to render them free from infection. It was, and still is, impossible to induce most of those who have had an attack of malaria to submit to frequent examination after they have once lost the fever, or to persuade them to continue the prescribed course of treatment. Naturally it was easier to ensure continuous treatment and adequate examination of the school-children ; few carriers were found among the children, and it seems that the majority of carriers are adults. With one exception (an infant who had quartan fever) all the cases examined had benign tertian fever ; a few imported cases of malignant tertian were seen, but this form of malaria did not spread.

As a result of the general rise in the prices of commodities after the war, treatment with quinine became very expensive, and there was some fear that the malaria station would have to be closed ; fortunately this was not found necessary, but its activities were considerably restricted.

Until 1919 only spasmodic and limited attempts were made to deal with the breeding places of mosquitoes ; the work was hampered by scarcity of labour and financial stringency. A few small swamps were filled up, and others treated with oil ; hibernating mosquitoes in rooms and cellars were destroyed by flame-projectors and insecticide sprays, but the work could not be done very thoroughly on account of the expense, and the operations were opposed by many of the people whose houses it was hoped to free from the insects. More progress was made in 1920 and subsequent years, but hibernating Anopheles mosquitoes were often found in dwelling-houses in very large numbers.

Besides *Anopheles maculipennis*, *A. bifurcatus* also occurs in East Friesland, but in too small numbers to play any important rôle in the spread of malaria.

Professor E. Martini has described three races of *A. maculipennis* in Germany, which are distinguishable from one another by the markings and colour of the eggs, and some other morphological features of the adults ; the differences are especially marked by physiological and ecological characters. In large lakes and rivers, the race *messeae* is prevalent ; *typicus* is seldom found with the other two, and only in a few localities, where there is cold spring-water. The commonest race, and almost the only one in the Emden district, is *atroparvus*, which is found along the whole seacoast from Emden to Danzig, and also inland, where brackish and saline water occurs. In Emden, among 700 specimens, only 30 belonged to the *messeae* variety, all the others being *atroparvus* ; *typicus* was not found at all. Although *atroparvus* is the mosquito concerned with the existence of malaria in Emden, it cannot be considered a particularly dangerous race, since it frequents long stretches of the German coast, and also inland places, where no malaria occurs. Indeed it is more zoophilic than anthropophilic, though it is not at all averse to biting human beings. It passes the winter chiefly in cattle sheds and pigsties, where the temperature is sufficiently high to enable the plasmodium to carry on its development, and to induce the mosquito to feed occasionally.

In Emden it was found that several cases of malaria usually occurred in the same family ; it was comparatively rare for a single member to be attacked. No doubt this is due to one or more persons acting as carriers, from whom the other members of the family derive their infection. For the same reason, the neighbours often became infected, and so small foci of malaria are formed.

During the 23 years dealt with in the report, the blood of 170 babies under one year was examined for malaria ; of these 57 gave positive results, the youngest infected infant being 10 weeks old. Although the disease is not common in old people, a woman aged 90, and a man aged 99, were found to have malaria.

In 1933, the last year of the period covered by the report, the blood of 751 persons was examined ; malaria parasites were found in 178 of these (23·7 per cent.) ; it is evident therefore that, although it is less prevalent than in many former years, endemic malaria is very far from being stamped out in the Emden district.

Dr. Friedrich GRUNSKE's account of the endemic malaria in Emden invites comparison with the history of malaria in similar districts in England. The conditions in Romney Marsh, the Isle of Grain and some other places, are not at all unlike those described by him in East Friesland, though the areas concerned are much smaller. On Romney Marsh *Anopheles maculipennis* is extremely plentiful, and many suitable breeding places exist, in spite of an extensive system of artificial drainage. In the autumn and winter the insects can be found in immense numbers in some of the older cow byres, stables, pigsties, rabbit hutches and similar places ; that they are not indisposed to bite man is shown by the fact that many people in these districts use mosquito nets. It is impossible to believe that the mosquitoes have no opportunities of becoming carriers of malaria ; within easy distance of Romney Marsh and the Isle of Grain, there are barracks and occasional concentrations of soldiers, many of whom have certainly been abroad, and of these it is very probable that some are carriers. Moreover, endemic malaria does occur in both places, though the number of cases is very small. Formerly these districts were notoriously malarious : why has malaria practically died out ? It is usual to attribute this to such factors as a higher standard of living, better housing and improved general sanitation ; doubtless these are largely responsible for the almost complete extinction of the disease. But there is also another change in the local conditions, which is of considerable importance, and which is liable to be overlooked. This is the great improvement that has taken place in the housing of cattle and other animals. The race of *Anopheles maculipennis* that is found on Romney Marsh, like that in the Emden district, is decidedly zoophilic. If it is desired to find mosquitoes, it is of little use to seek for them in the light and airy modern cow sheds, provided as these are with free ventilation, drainage, clean whitewashed walls and tiled roofs ; very few mosquitoes will be found in these. But there still exist, on some of the farms, old-fashioned, dark, damp and stuffy byres and stables ; in such places Anopheles mosquitoes abound, as the conditions suit them admirably. Dr. GRUNSKE refers to the many animals, cows, pigs and goats, kept in close proximity to the houses of many of the inhabitants of the Emden district and it seems likely that further improvement in the amount of malaria would occur, if attention were given to the housing of domestic animals. This would probably have more effect in diminishing the number of mosquitoes than attempts to do away

with the breeding places, since, from the nature of the country, this can only be done partially ; and, unless all the breeding places over a very wide area can be abolished, no very decided diminution can be attained.

The general lines of successful antimalarial operations are well known by now ; Dr. GRUNSKE has done good service in drawing attention to the practical difficulties that may be met with, when an attempt is made to carry them out, and his very interesting report is of much wider application than to Germany alone. *H. J. Walton.*

VELLARD (J.). **Le venin des araignées.** [Spider Venoms.] Préface du Professeur Caullery.—311 pp. With 63 figs. Monographies de l'Institut Pasteur. 1936. Paris : Masson et Cie, 120, Boulevard Saint-Germain. [45 fr.]

It has been known for many years that the bites of spiders of the genera *Lactrodectus* and *Glyptocranium* often have serious consequences for man and domestic animals, especially in Italy and Southern Russia ; of late, other spiders have been incriminated in North and South America, Madagascar, Australia, New Zealand, and, to a less extent, in the countries bordering the Mediterranean. Dr. Vellard has now considerably extended the list of dangerous spiders : he has had exceptional opportunities for the investigation of araneism, as he has worked at the Butantan Institute (São Paulo) for several years, and has travelled in other parts of South America, where spiders of many families are particularly common and much feared. Moreover, he is a naturalist, as well as an experienced experimenter, and he has devoted special attention to the identification of South American spiders, their habits and venoms.

In this book so many interesting and important facts are recorded that it is impossible, within the limits of a review, to do more than allude to a few of them ; the whole book well repays careful study.

The results of the bite of a spider are often unrecognized as such. In Brazil the very serious nervous symptoms caused by several species of *Ctenus* have been mistaken for tetanus, and the ulcerations caused by *Lycosa* have been regarded as cases of leishmaniasis or as tropical phagedaenic ulcers.

Some of the negative results recorded in experiments with spider venom may be due to the fact that a spider may bite without injecting any venom, although there is plenty in the poison glands ; of this fact the author gives a good example. Many spiders show marked specialization in their venom, which is much more toxic for the spider's habitual prey (particular groups of insects, aquatic animals, lizards, etc.) than for other animals.

Some observers have found spider venom to be acid, and others alkaline. To settle this matter, Dr. Vellard examined a large number of spiders ; he found that the venom of the same spider is sometimes acid and sometimes alkaline. The species, age, sex, and state of activity of the reproductive organs have no influence on the reaction ; prolonged fasting tends to acidify the venom. But the chief factor concerned is the atmospheric temperature ; at Rio de Janeiro, for instance, almost all the spider venoms are alkaline during the warm season ; in the cool season the reaction is often acid. In a lesser degree there is the same variation in the reaction of the haemolymph. Normally this is alkaline, but in cold weather it may become neutral

or slightly acid; sometimes the venom is acid, and the haemolymph alkaline.

The venoms which possess the property of producing gangrene are much more numerous than those which are purely neurotropic; the author gives several photographs of the lesions caused by the bite of *Lycosa raptoria*, which show extensive sloughing and ulceration of the skin over wide areas.

Haemolysins have not been found in spider venom, but are obtained from the body and eggs of several spiders, whose bite is relatively harmless; they cannot be obtained from all spiders, nor, at all seasons, from the same spider. Their presence is intimately associated with the reproductive activities of the female; they are not found in male spiders, nor in the female unless fecundated. Haemolysins appear with the development of the eggs and disappear when these have been laid; they are also found in the eggs and in very young spiders. Antigens may be produced by suitable injections into animals, but antisera prepared in this way are specific, and do not protect against the venom of the same spider; the converse is also true.

The haemolymph of spiders is toxic, and this toxicity is constant and independent of sex, reproductive activity, or the acidity or alkalinity of the fluid. The symptoms produced in animals by the injection of the haemolymph are very uniform in the case of all the species studied by Dr. Vellard; when given intravenously it produces almost immediate dyspnoea, followed soon by apnoea, a few convulsions, and death.

More than half of the book is occupied by a systematic account of the different families of spiders met with in South America, their venom, and its mode of action, with many clinical reports of cases of spider bites in man. This is, perhaps, the most important part of Dr. Vellard's book, and it will long remain a valuable record of his work.

In the third part of the book descriptions are given of the methods of treatment of spider bites and the preparation of antisera. These antisera are highly specific, and it is unfortunate that, in so many cases, the spider is not identified, a fact which limits the use of the serum.

Dr. Vellard's monograph bears abundant evidence of his industry and enthusiasm, and it is written in the easy and attractive style that is so often associated with the best French scientific literature.

H. J. Walton.

Ghosh (Birendra Nath) [F.R.F.P. & S. (Glas.), etc.]. **A Treatise on Materia Medica and Therapeutics including Pharmacy, Dispensing, Pharmacology and Administration of Drugs.** 14th Edition.—pp. xv+724. With 13 figs. 1936. Calcutta; Hilton & Co. and London: H. K. Lewis & Co., Ltd. [Rs. 7 As. 8 or 12s. 6d.]

Only three years have elapsed since the preceding edition of this work was published—proof that the book still fulfils its mission. This new issue is, nevertheless, a great improvement on the last; fairly extensive revisions have been carried out, notably in sections dealing with anaesthetics, narcotics, quinine and the vitamins; accounts of others have been introduced, notably dilaudide, dicodide, evipan, percaine, coramine, carbarsone, vioform and antivenenes; slight rearrangement of the matter is also, we think, an advantage, in particular transference of the section on Pharmacy and Dispensing to the end. A very

valuable section is that dealing with incompatibility, for it is astonishing to those medical men trained some 30 years ago or more to find how little the modern student knows of this subject. Dispensing having to a great extent gone out of fashion for the general practitioner, he does not realize how nauseating are some of the mixtures he prescribes, and how he inadvertently may prescribe some explosive or poisonous mixture. The tablet and patent medicine manufacturer has certainly saved the busy practitioner a lot of time and trouble, but at the same time he is largely responsible for the widespread ignorance of dispensing and pharmacology exhibited by the more recently qualified medical man.

Among the new additions it is surprising to find no mention of venoms as haemostatics, especially as they have proved their value and the literature during the past year is fairly extensive. Misprints are few, we note that *histolytica* is still wrongly spelt. The list of " contractions of phrases used in prescriptions " needs revision ; does anyone nowadays write *omni bihora* for " every two hours," and even Smith minor would be rightly caned for " Ante cibus," " post cibus," " in pilulae xii divide." The format of the book is much improved by a larger page and clearer type. *H. H. S.*

SABADINI (L.). **Les kystes hydatiques de la rate.** [Hydatid Cysts of the Spleen.] Préface du Professeur Costantini.—200 pp. With 82 figs. 1936. Paris : Masson & Cie, 120 Boulevard Saint-Germain. [32 francs.]

Hydatid cysts of the spleen are rare, constituting between 2 and 3 per cent. of all hydatids, according to the records of most authors. Nevertheless the spleen comes third in the list of individual organs invaded, though a long way behind the liver, which of course heads the list, with some 75 per cent., the lung coming next with 10 per cent. Partly, perhaps, on account of its rarity, partly by reason of its surgical importance, there is a considerable literature dealing with the condition. The bibliography appended to this book names nearly 300 references.

After a few short remarks on the prevalence and history the author describes in a few pages the pathogeny of primary and secondary involvement of the spleen by hydatid. The chapter on the pathological anatomy which succeeds this is fuller and of much interest and is illustrated by a number of explanatory diagrams mostly from Professor DÉVÉ's work. The clinical section, as would be expected, is not a long one, for after all there is not much to be said on the clinical aspect. As regards diagnosis, beyond the physical signs, mention is made of Casoni's test and complement fixation. Two chapters, the fullest and rightly so, are devoted to treatment and the details of operative procedure ; this is abundantly and clearly illustrated. Finally, there is a chapter of " observations." This consists of brief accounts of patients, some under the author's care, others culled from the literature, together with remarks upon certain of the cases.

The monograph summarizes the literature and present knowledge of the subject and should prove a useful work of reference both for the general practising clinician and the surgeon. *H. H. S.*

Printed under the authority of HIS MAJESTY'S STATIONERY OFFICE,
By The South Essex Recorders, Limited, High Road, Ilford.

(1465) Wt. P2/166 1875 10/36 S.E.R. Ltd. Gp. 353.